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Vol. XIV, No. 3 MARCH, 1925

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

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THE SEVENTY-THIRD ANNUAL CONVENTION OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN DES MOINES, IA., DURING THE WEEK OF AUGUST 24, 1925.

The 1925 Meetings of the American Conference of Pharmaceutical Faculties and the National Association of Boards of Pharmacy will also be held in Des Moines, during the week of August 24, 1925.

For Association Roster, see page x.

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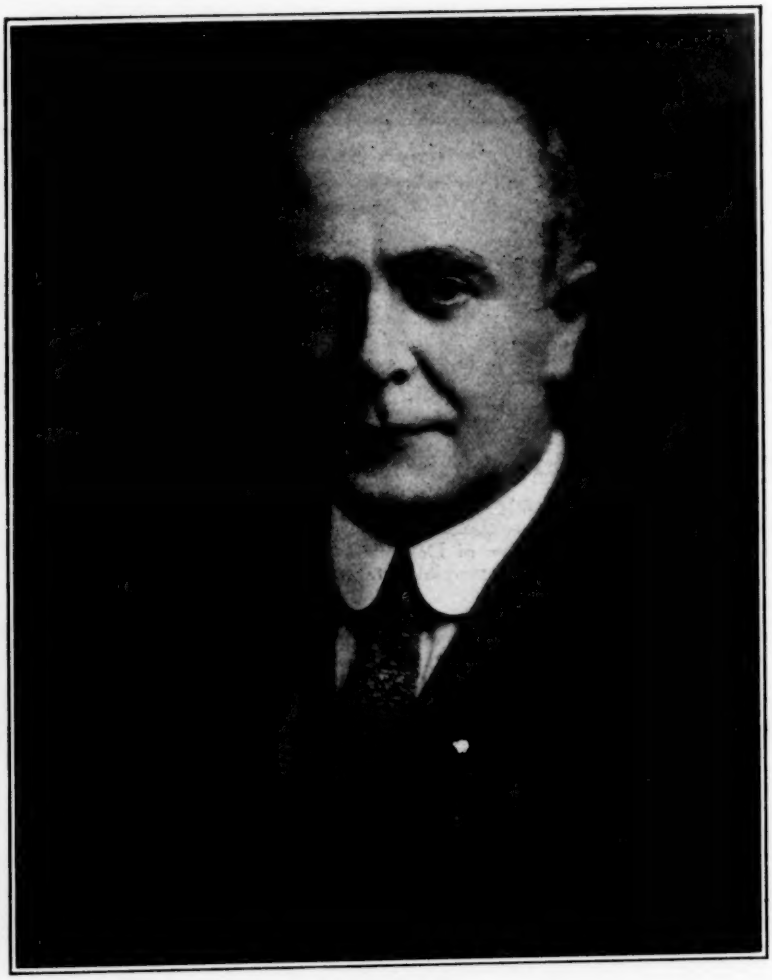
WALDEMAR BRUCE PHILIP

SAN FRANCISCO, CALIFORNIA

Chairman of the House of Delegates, A. Ph. A. and of the Section on Commercial Interests, 1924–1925



W. BRUCE PHILIP.

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XIV MARCH, 1925 No. 3

WALDEMAR BRUCE PHILIP.

The family history of the Chairman of the House of Delegates, A. PH. A., complements his pharmaceutical record. Mrs. Philip is a graduate in pharmacy of the University of California; the children—Mercedes L. and Harold M.—have been registered as pharmacy apprentices; the former is a freshman at the University of California, and the latter is attending High School.

Mr. Philip's affiliations speak for his attachment to pharmacy, and he has further proven his loyalty to institutions where he received instruction in the science and art of pharmacy. After graduating from Sacramento High School, the young man matriculated in the Pharmacy Department of the University of California and was graduated in 1901; thereafter, he attended New York College of Pharmacy, where he earned the degree of Phar.D. He studied so as to render service; therefore, in more recent years, he completed the law course at Hastings College of Law, University of California, receiving the degree of LL.B. in 1923.

Mr. Philip was born in Sacramento, July 19, 1878. He served as apprentice in the pharmacies of O. P. Willis, Sacramento; George H. Munroe, Fresno, and Dr. Albert L. Scholl, San Francisco. He is a member of the firm of Willis & Martin Co., Sacramento, and Philip & Philip, of Oakland.

It will be noted that associated activities are regarded as necessary as individual endeavors by the Chairman of the House of Delegates, A. PH. A., who is also Chairman of the Section on Commercial Interests. He has been Vice-President of the AMERICAN PHARMACEUTICAL ASSOCIATION, Associate and Secretary of its Section on Commercial Interests. He has served as Secretary of the Retail Druggists' Association of San Francisco for four years, of the Alameda County Pharmaceutical Association for five years; he is an Ex-President and a past Vice-President of the latter organization; has been a member of the Executive and Legislative Committees of California Pharmaceutical Association for twelve years, and by successive Vice-Presidential steps gained the office of President.

He is a member of the National legislative committee of the National Association of Retail Druggists, and has held the offices of first, second, and third Vice-President in that association. Few, if any, secretaries in the San Francisco Society of Secretaries hold membership by virtue of more secretarial attachments than Mr. Philip.

Ten years ago his *Alma Mater* elected him member of the Board of Trustees; for four years he has been Instructor in Commercial Pharmacy, and three years ago he was elected Instructor in Laws of Pharmacy. He dedicated the Searby Memorial Chair[1] in Greek Theater, University of California. He is a past Vice-President and President of the Alumni Association; has been a grand officer of Kappa Psi, pharmacy fraternity, for ten years; is a member of Phi Alpha Delta, legal fraternity; is affiliated with and an officer of distinction in the Masonic bodies and Knights of Pythias, and is Educational Lecturer of the Masonic Grand Lodge of California.

Mr. Philip is a member of the Athens Athletic Club, San Francisco Ad Club, San Francisco Bar Association, Commonwealth Club of California, and of the State, San Francisco and Oakland Chambers of Commerce.

"We live not to ourselves, our work is life" is expressed by the activities of Waldemar Bruce Philip, and this record, although incomplete, will at this time serve the purpose of a sketch. E. G. E.

HOME SIGNIFIES STABILITY AND SECURITY.

BY DR. JACOB DINER.*

History records that during the Nomad days society, education and the safety of the individual were at low ebb. Civilization, with all it implies, began with the building of the first permanent domicile, resulting in the gradual development of village, town and city with the necessary laws and ordinances to give stability to the home and security to the individual.

Pharmacy, in all its branches and ramifications, has led and is still leading a Nomad life. No resolutions at State or National conventions can give it the stability, the power to advance in knowledge, and the promotion of public welfare, so long as our efforts are scattered and our stability is questioned and questionable. To concentrate in our altruistic work, to coöperate with each other in the up-building of our beloved profession, to act as a unit in promoting public welfare and to have a voice in public affairs we must prove our stability and our ability to do so.

It has been said that the main reason why the United States of America need not fear a country-wide uprising is because America is a land of Homes—again demonstrating the need of a home and its implied safety. For these, if for no other reasons pharmacy needs a permanent home and every pharmacist should feel that in contributing to the building of our permanent Headquarters he is actually building his own home.

"Twice gives he who promptly gives."

---

[1] William M. Searby, President of the AMERICAN PHARMACEUTICAL ASSOCIATION, 1907–1908; born January 21, 1835; died October 7, 1909.

* Dean Pharmacy Department, Fordham University.

EDITORIAL

E. G. EBERLE, EDITOR 253 Bourse Bldg., PHILADELPHIA

THE FIGHT TO CURB NARCOTIC ADDICTION AND THE WORLD'S PRODUCTION OF NARCOTICS.

THE relation of the world's production of narcotics to the quantity required for medicinal and scientific uses, which may be more or less approximately ascertained, provides data which have some value in determining the extent of "illegitimate" consumption of narcotics and the number of habitués.

The purpose of the editorial in the February issue of the JOURNAL was to direct attention to the interest pharmacists exhibit in regulations applying to the dispensing of narcotics; the aim of this comment is to impress the need of being more exact in expressing the figures of narcotic production and narcotic addiction—a constant holding up of exaggerated statements gives misinformation which, like all untruths, does injury to the cause. Facts may be disappointing, but they convey knowledge, and are essential for all good work—truth points the way to results. All that is undesirable may not be corrected by a dictum, when the evil influences have been in force for generations, but a knowledge of facts, sympathetic coöperation, and a resolve to discountenance selfish promotions, will assure results. Unquestionably, habitués, as well as those who encourage addiction in any way, need a shock to awaken them to a realization of what the world expects of them—not to shackle, but to subserve.

The term "illegitimate consumption" is not given the same meaning by all individuals or nations. The attitude in this country is that the term "legitimate use," as it applies to narcotics, should be restricted to those for medicinal and scientific purposes. The interpretation may be affected by habit, greed, production, the belief that progressive suppression is possible and that it is "impractical to eradicate over night the ingrained habits of millions of Orientals." Restricted measures may, in a degree, rightly be given a different meaning by a nation at home than in its possessions. Observation changes with the viewpoints—here the habitués are invalids, inmates of asylums or charitable institutions, criminals, etc.; elsewhere, it has been said, these represent a minority, and the greater number, though slaves to the habit, are active in various pursuits, including the cultivation of the poppy. Discussions along these lines have appeared in the public press. Certain countries have situations to contend with that the United States, fortunately, has not. The former should not receive all the blame for the failure of the Opium Conference. It reflects great credit on the United States that narcotic addiction has been curbed to a very great extent in the Philippines—it serves as an example of what may be done in other sections of the world, where, in addition, the economic aspect enters into the problem.

While the dangers of narcotic addiction should never be minimized, there is great need for the press to discriminate between authentic data on the production and use of narcotics. Seldom are the values of narcotics seized given in the newspapers at less than $10,000, and $100,000 is not an unusual sum. These figures

are generally computed on the basis of $1.00 to $2.00 per grain of morphine sulphate, which may be the price peddlers receive from the unfortunates. The price on morphine sulphate, in legitimate trade, is about $11.00 per ounce, or approximately $2^1/_2$c per grain. Startling figures are put forth by propagandists who, perhaps, desire to come into the limelight, have some other motive, or become so obsessed with their ideas on the matter that their judgment becomes biased. The Federal Government now has accurate data, as far as this country is concerned, and reliable information can be obtained from the Opium Committee of the League of Nations relative to the status of the use of these drugs in the world at large. Bulletins No. 924, by L. Kolb and A. G. DuMez, and 956, by A. G. DuMez, on "The Prevalence and Trend of Drug Addiction in the U. S., and Factors Influencing It," and "Per Capita Medicinal Requirements of Narcotics,"[1] may be had from the Government Printing Office.

A statement frequently has been repeated that the *per capita* consumption of opium in the United States is greater than that of any other country. The *per capita* consumption in these statements is given as 36 grains of opium—the figure given out by the Special Committee of Investigation of the Traffic in Narcotic Drugs appointed by the Secretary of the Treasury March 25, 1918. This figure was arrived at by dividing the average annual importations for the five-year period ending June 30, 1915 by the population of the U. S. for 1910. This covers a period prior to the enactment of the Harrison Law, when narcotics were still constituents of proprietary cough and soothing syrups, diarrhoea mixtures, etc. At present the *per capita* consumption is about 8.7 grains of opium (probably somewhat less), and considerably lower than that of many other countries. To meet this requirement the Narcotic Board of Control of the United States has fixed the amount which can be imported annually at 130,000 pounds. The *per capita* requirements, for all countries, as estimated by the Committee on Hygiene of the League of Nations, are approximately 7 grains of opium and $^1/_{93}$ of a grain of cocaine.

There are two principal forms in which opium is used by addicts—its alkaloids, as in this and other occidental countries; raw or prepared for smoking, as in oriental countries. The sources differ—the former is opium with a large percentage of alkaloids, produced in Europe, the Near and the Middle East; the other, low in alkaloids, is grown in India, China, etc. It may be assumed that the latter is used almost exclusively for smoking, as it is not a profitable source of the alkaloids, under ordinary conditions. The figures for the medicinal needs deducted from the total production of "high grade" opium practically give the amount consumed "illegitimately" in the occidental countries, and from this the number of addicts may, in a way, be arrived at. Without going into the details of the calculation, the number of addicts for the United States on this basis would be less than 50,000, but allowing for leaks, let us say double that number.

The accepted method of estimating the amount of smuggled material, used by the Advisory Committee on Opium of the League of Nations, is to assume that the Customs seizures are equal to 10 per cent. of the amount smuggled into any country—in other words, the total amount of material smuggled into any country is ten times the amount which is seized by Customs officials.

---

[1] See JOURNAL A. PH. A., October, 1924, p. 987.

In the fiscal year 1922, there were seized by United States officials 49,381 ounces of smuggled opium, 24,902 ounces of morphine sulphate, 1,451 ounces of heroine hydrochloride, and 19 ounces of codeine—the equivalent of 16,273 pounds of opium. Ten times this amount, or 162,730 pounds, would then represent the probable total of smuggled material on an opium basis. This would have supplied 70,000 addicts, in round numbers, with their daily dose of opiate for a year, and figured not so different from the preceding. The curtailment of the production of opium in the countries which produce only medicinal opium will not eliminate smuggling. It may, on the other hand, make the problem of smuggling a great deal more difficult to deal with by making it profitable to produce opium alkaloids and their derivatives from low grade opium.

Poppy cultivation and opium production, and sale and export of opium, are under strict government control in India. China is the largest producer of opium (low grade), and the central government is not now in position to enforce its demands relative to opium production.

On account of the length of this comment, only this will be said relative to cocaine—if the total world's production of coca leaves for 1922, 3,800,409 pounds, had been used solely to supply addicts, the number would have represented only 67,720 with a 6-grain daily dose of cocaine hydrochloride.

The narcotic supply, opium alkaloids and cocaine for habitués, unless supplied in a legitimate way or from legitimate sources, comes from illegitimate dealers whose supplies are smuggled into the country, and the suppression of smuggling constitutes the greatest problem in dealing with these drugs, here and in all other occidental countries.

There is no desire to minimize the seriousness of drug addiction; the most watchful care and study must constantly be given the subject or the addiction may increase—distributors and users are secretive. Violators should be given a punishment that will discourage them and also others who would engage in the traffic. Having said this, it is encouraging to note that drug addiction in this country is becoming a less important problem each day. The extent of addiction has been on the decrease since the beginning of the enforcement of the Harrison Antinarcotic Act in 1915, is still on the decrease, and will no doubt continue to decrease to a time not many years distant, let us hope, when the remaining addicts will be persons taking opium because of an incurable disease and addicts of the psychopathic, delinquent type, who spend a good part of their lives in prison.

E. G. E.

NOMINATIONS FOR THE HALL OF FAME.

The public nomination of candidates for the Hall of Fame of New York University closed March 15.

The names received will be submitted to the Senate of the University and then to a Committee on Nominations. This committee, designated by the Senate, is made up of twenty-one electors, and the names selected by it as worthy of a place on the final ballot will be submitted about June 1 to the full College of Electors. This electoral body includes approximately 100 men and women, from all parts of the country, who are well known in scientific, judicial, political, literary, art and diplomatic cricles. It requires a vote of three-fifths of the electors to fill a niche in the Hall of Fame.

AMERICAN CONSULAR SERVICE AND CUBAN PHARMACEUTICAL ASSOCIATION ACT PROMPTLY ON WRONGFUL USE OF THE NAME OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

REFERENCE to page 999, November JOURNAL A. PH. A., 1924, will inform the members of the watchfulness of the American Consul, Mr. Frank Bohr, in protecting the good name of the AMERICAN PHARMACEUTICAL ASSOCIATION, and a communication, made part of this comment, discloses the deep interest exhibited by the Cuban pharmacists in this matter. The thanks of the ASSOCIATION are due Mr. Bohr and an expression of good wishes and esteem is conveyed to Secretary Dr. B. Rumbaut and his colleagues. The prompt action and the professional interest evidenced in the letter herewith, of December 30th, was expected, as indicated in the first paragraph of the comment on p. 999. There exists the regard which obtains in professions and this is strengthened by the attachment of our friends in the Spanish-speaking countries. They may be assured that their communication is most welcome.

The decisiveness of the Cuban Board of Health and the American Consul General should also be recorded in these pages, and this probably will close the incident. The letter of Dr. B. Rumbaut, Secretary, as translated for the JOURNAL by the Cuban Consul, at Philadelphia, follows:

PHARMACEUTICAL ASSOCIATION OF THE JUDICIARY DISTRICT OF CIENFUEGOS.
(CUBA.)

December 30th, 1924.

"Mr. William B. Day, Secretary,
American Pharmaceutical Association,
Chicago, Ill.

"Distinguished colleague:

"This body of associates, in its meeting held on the 21st inst., passed unanimously a resolution to send to you this communication, signifying our protest before that Association against the fact of a pharmacist established in this City unlawfully using the mark ESPECIFICO BRENOT which really is a registered trade mark for a patent medicine quite another from which he actually used.

"We know that this action has been denounced to the concerned sanitary authorities and that every step has been given against the usurper, but nevertheless we want to express through this way to that Association our uncongeniality with such actions *which affront our noble profession.*

"We beg to introduce this expression of our feelings to that Institution in its next meeting, and remain

"Yours very sincerely,
(Signed) DR. B. RUMBAUT, *Secretary.*"

The letter from the American Consul, Mr. Frank Bohr, is appended:

AMERICAN CONSULAR SERVICE.

Cienfuegos, Cuba, January 27, 1925.

"Mr. William B. Day, Secretary,
American Pharmaceutical Association,
Chicago, Illinois.

"Sir:

"I have to refer to your letter of October 15, enclosing copy of one addressed to the Director de Sanidad at Habana, regarding the preparation, Especifico Brenot understood to be pre-

pared by the druggist Jose Fernandez Valdez of this city and in view of your statement that you are not in a position to go to expense in order to institute proceedings in this case, I transmitted copies of our correspondence to the American Consul General and the Ambassador at Habana, in case it be considered advisable for the latter to make official representations in this case to the proper authorities of the Government at Habana.

"And in reply I am now in receipt from the Consul General of a copy of a communication dated the 7th instant by the Secretary of Sanidad, indicating that the matters as stated with reference to the manufacture of this product had been confirmed and that the stock of 24 bottles found in the possession of this druggist was confiscated and a fine of $25 assessed against him; that he claimed to have purchased the product from a certain Oscar Smith whose whereabouts were unknown.

"I have also ascertained that the product mentioned is no longer being offered for sale with labels to indicate that your Association is the manufacturer but now rather with labels which do not indicate the name of the manufacturer but give the name of the druggist, Jose Fernandez Valdez as the general agent for Cuba.

"I am, Sir,

Very respectfully yours,
(Signed) FRANK BOHR, *American Consul.*"

"UNITED WE STAND—DIVIDED WE FALL!"

UNDER above caption a message has been prepared and sent to the Headquarters' Campaign Committee by Dr. A. R. L. Dohme. The title expresses a hope, and a timely submonition adds strength to the precept which should appeal to A. PH. A. members and pharmacists generally. Rather than lose the force of the writer's diction by presenting the comment in abstract, the greater part of the contribution is printed herewith. A definition of *morale* is "belief in one another;" it may be applied here because the contributor expresses his belief by word and action. Parts of the message follow:

"The medical profession has gained in strength and influence every year since it became united in the American Medical Association, and despite criticisms leveled at the A. M. A. and its control and management by many people, the medical profession, as a profession, is strong in progress, research, influence and lucrativeness for its members. All of this has been made possible only through organization and coöperation.

"It is unquestionably true that when organizations become huge and lucrative as corporations, as for instance chain-store enterprises, capitalists and bankers enter into the game and very soon exert their influence, and control of a situation is apt to result. This danger is not vital to a strongly organized industry which is very much diversified, as is the drug industry with its three branches of manufacturing, jobbing and retailing. Be that as it may, it is by no means as important or vital as is the absence of organization and coöperation, as at present, for this absence renders the industry vulnerable and keeps it down, and prevents it from progressing. * * *

"Every sick person, in order to get well, depends upon the physician to diagnose his sickness, and upon the druggist to properly dispense drugs of the proper purity and quality to combat the illness successfully. This is a great responsibility, and the public should know it, but unfortunately does not, for the retailer, alone, does not have the time nor the means to inform the public.

"So that the profession of pharmacy may really stand for something and be talked of in the press, in the halls of legislation, and by the people, it is necessary, among other things, that they have a big and representative home, preferably at Washington (where most of the legislation and control that concerns the drug trade is located), and from that home have all publicity, research, and progressive work in the profession emanate. Reporters will go there, the news will be sponsored, legislation will originate and be pushed from there, and meetings will be held there. This home should be impressive and beautiful to attract the attention of all visitors, and be pointed out by guides to tourists, and should be extensive and roomy enough to properly house all the branches of the drug trade, research laboratories, halls for lectures and meetings of associations.

"The best thing that could happen for pharmacy, in all its branches, would be the successful completion of the funds needed to construct the Pharmacy Building and endow it sufficiently to enable it to function properly and, when completed, result in a successful federation of pharmaceutical associations, all united in one purpose—to help pharmacy attain the standing and respect in the public mind that its importance to life and health justifies.

"Large corporations and institutions help the country, collectively—pharmacy helps each individual many times in his life, individually. The doctor is worthy of his hire for he saves the life by diagnosing disease and applying the right remedy, and the pharmacist is worthy of his hire for, unless the remedy is properly dispensed and is of the proper purity and condition the patient may die despite the proper diagnosis and treatment.

"The writer has agreed to equip in that home of Pharmacy a research laboratory as a memorial to his father and uncle, Charles E. Dohme and Louis Dohme, two pioneers in the retail, manufacturing, and college of pharmacy history of this country. Here quite a number of competent, trained, pharmaceutical chemists will be equipped to work out many problems in years to come that may and, probably, will prove of importance and value to pharmacy and humanity. This laboratory cannot be realized and fitted out until the headquarters is built, and this cannot be done until the money is subscribed. Therefore, pharmacists—get busy, one and all should subscribe to this fund, for no money you ever gave to a worthy cause will mean as much to you and your standing as a pharmacist as the money you subscribe to the Pharmacy Headquarters' Building Fund."

CHANGE OF MEETING DATE OF THE DES MOINES CONVENTION.

It has become necessary to change the convention days of the 1925 meeting of the AMERICAN PHARMACEUTICAL ASSOCIATION, American Conference of Pharmaceutical Faculties and National Association of Boards of Pharmacy from the week beginning August 31 to the week beginning August 24. It will be more convenient for the Local Committee to arrange for the convention at that time, for the attendance at the State Fair during the time first selected would have made it somewhat more difficult to secure accommodations. While not decided upon by vote of the Council, at this writing, in all probability the meeting will be held during the week of August 24, 1925.

THE STATE OF SILVER IN PROTARGOL (ARGENTI PROTEINATUM) AND COLLARGOL (COLLOID SILVER; ARGENTUM CRÉDÉ).*

BY I. M. KOLTHOFF.[1]

I. The use of silver nitrate (*stone of hell; lapis infernalis*) has been well known in medicine for a long time. There are, however, several objections against its application; for example, it is reduced in the body to metallic silver, which is deposited, especially, in the cells of the skin. The consequence of this is that the latter becomes blackened, giving the patient a dark appearance. This black color, called argyria, may last for years, even during the whole life of the individual affected. The color may even be so intensely black that the patient resembles a negro. Th. Paul refers to the case of a clergyman in the army who was treated for such a long time with silver nitrate that coloration became so complete that the Queen of Sweden, observing the man, asked in astonishment, why a negro had been appointed as a clergyman?

After Lister had discovered the antiseptic treatment of wounds, silver solutions were applied for that purpose, especially to the infected mucous membranes. The silver nitrate solutions appeared to irritate the tissues in a very disagreeable way, hence the endeavor to prepare difficultly soluble or complex silver preparations. It was not until 1894 that Schering succeeded in preparing a silver compound of this kind, which was marketed under the name of Argentamine; it contains silver phosphate in aqueous solution of diethylenediamine and is still used in the treatment of gonorrhœa. In the same year (1894) Heyden in Radebeul (near Dresden) prepared the well-known Collargol, which contains the silver in a colloidal state. It is also called colloidal silver or Argentum Crédé, as Crédé was the first to point out how to prepare this colloidal silver.

In 1895 Argonin, a silver caseinate compound, was recommended for the treatment of gonorrhœa; and at last, in 1897, Friedrich Bayer & Co. prepared the well-known Protargol—Argenti proteinatum. According to the description by this Company, it is a silver-proteid compound with a silver content of 8.3 per cent. The great advantage of this preparation is, that it has no irritating action and a concentrated solution can be prepared of it (50 per cent.). Since then a great many colloidal silver preparations have been put on the market; Th. Paul[2] in 1912 gave a list of 52 silver preparations used in medicine, and since that time this number has increased very rapidly. During the last few years preparations have been employed in which the silver occurs in the presence of other metals.

II. A very interesting investigation relative to the action and the properties of colloidal silver preparations has been carried out by Theodor Paul.[2] Some of the results of his researches are as follows:

A. The bactericidal potency depends on the magnitude of the silver-ion concentration of the solution and its ability to split off new silver ions, when the latter are removed in any way. So if we express this action in modern terms, we could say that the bactericidal potency depends on the buffer-action of the preparation for silver ions.

---

* Presented before Scientific Section, A. PH. A., Buffalo meeting, 1924.

[1] University of Utrecht, Holland.

[2] Th. Paul, *Z. Elektrochem*, 18, 521 (1912).

B. The preparations or their solutions must produce mixtures with the organic tissue liquids and aqueous solutions of proteids, bases and acids, and should not give precipitates with them.

C. The silver-protein compounds are more soluble than silver chloride, by an excess of sodium chloride they are transformed into silver chloride.

D. In diluting the colloidal silver preparations we may distinguish three cases:

a. The silver-ion concentration decreases. This is the case with Protargol. A 1 per cent. solution has a silver-ion concentration of 8×10^{-3}, a 0.31% solution of 1×10^{-3}.

b. The silver-ion concentration remains constant. This is the case with Sophol, the solution of which has a ($Ag^{\cdot}$) of 2×10^{-5}.

c. The silver-ion concentration increases. Such is the case with Collargol, Argentamin, Lysargin. A 4-per cent. Collargol solution has a ($Ag^{\cdot}$) of 1×10^{-4}; a 0.25 per cent. solution of 2×10^{-3}.

I wish to remark here that it was possible for me to confirm Paul's statement about the Protargol, but not relative to Collargol, as I will show later.

According to my opinion and experience, it is not quite certain that the bactericidal potency only depends on the magnitude of the silver-ion concentration, as Paul and Krönig concluded from their well-known investigation. In working with colloidal solutions, it may be expected that this bactericidal action also largely depends on the fineness of the silver particles, so that finely dispersed suspensions of silver chloride, bromide and iodide also may have a good action. Some preliminary experiments carried out in our laboratory confirmed our expectations in this respect. From a bacteriological point of view this matter is important enough to be investigated thoroughly.

III. The accurate composition of Protargol and the method of preparing it are not well known. H. V. Arny[1] states in his well-known book, "Principles of Pharmacy:" "Commercial products are usually prepared containing small amounts of proteids; such compounds having been found to yield more stable solutions. Among the proprietary forms of colloidal silver may be cited protargol and argyrol. These are now largely used in the form of glycerinic solutions for throat troubles." (The application in the treatment of gonorrhœa also may be mentioned.) Neither Schmidt ("Lehrbuch der pharm. Chemie," 1919) nor Hager gives satisfactory information about these preparations.

Only S. Fränkel[2] informs us that Protargol is obtained by precipitating a peptone solution with silver nitrate. The precipitate is warmed with protalbumoses and the solution evaporated to dryness. Though the prescription is very vague, we succeeded in our laboratory in obtaining good preparations of Protargol.

The silver proteinate may also be prepared by the action of moist silver oxide on albumoses.

From the above it may be concluded that the silver in Protargol is not present in the metallic state, but that it is in some way (chemical and colloidal) combined with proteids. This is not the case with Collargol, which is practically metallic silver in a colloidal state. It is prepared by adding silver nitrate to a solution of

[1] H. V. Arny, "Principles of Pharmacy," second edition, 1920, p. 565.

[2] S. Fränkel, "Arzneimittelsynthese," 1919.

ferrous sulphate, sodium citrate and sodium carbonate. A brown precipitate containing 97 per cent. of silver results and this, after washing free from impurities with ammonium citrate solution, is soluble in water or 10 per cent. sodium chloride solution. In all probability it contains a little gelatin as a protecting colloid. According to the data given in the literature, the silver content ranges between 75 and 98 per cent.

IV. The Protargol used by me was an original preparation of Bayer. The water content is not easy to determine, as the dried substance is very hygroscopic and the residue loses its last traces of water very slowly. We found a water content of 9.87 per cent. (after drying for 35 hours), which is a higher proportion than most pharmacopœias allow. According to the description of Bayer and most pharmacopœias the soluble silver content is stated to be between 8 and 9 per cent. (refers to the dried substance). We, however, found in the original substance a soluble silver content of 7.08 per cent., corresponding to 7.77 per cent. in the dried substance. The total silver content, however, was higher and appeared to be as high as 7.87 per cent. corresponding to 8.65 per cent. in the dried substance. In contradiction to the description given in Bayer's papers and in different pharmacopœias, I found that the original preparations all contain silver chloride. From the above could be concluded that the dry preparation used by me contained (8.65–7.77) = 0.88 per cent. silver as silver chloride. In order to check these results, we determined the silver in the insoluble residue that remained after the treatment with nitric acid and washing out with water.

In agreement with the above result we found, by means of direct analysis, a quantity of silver present as silver chloride corresponding to 0.85 per cent. Hence, it seems to me that the pharmacopœias must admit a definite amount of chloride in Protargol.

We have also determined the *N*-content of the Protargol; it contained 13.8 per cent. in the original substance, or 15.2 per cent. in the water-free substance. It is very peculiar that in carrying out the destruction with sulphuric acid without a catalyzer, the liquid soon becomes clear and colorless. In our determination this was the case after two hours, but the destruction was not complete, as all nitrogen was not present in the ammonium state. When the distillation was carried out after a destruction of two hours, we found the *N*-content 1 per cent. too low.

The Collargol used by us was a common commercial preparation. It contained no more than 67 per cent. silver, while 4.8 per cent. was present in the halide state.

V. As the magnitude of the silver-ion concentration seems to be of value in connection with its action as a remedy, I determined this concentration by means of a potentiometric measurement with a silver electrode. In the following table the data are given. The measurements are carried out with solutions of Protargol and Collargol:

Protargol. Concentration Protargol in per cent.	Silver-ion concentration.	Collargol. Concentration Collargol in per cent.	Silver-ion concentration.
1.4	2.9×10^{-3}	1	3.1×10^{-4}
1.0	2.8×10^{-3}	0.5	2.4×10^{-4}
0.5	2.0×10^{-3}	0.25	1.7×10^{-4}
0.25	1.2×10^{-3}	0.1	1.15×10^{-4}
0.1	0.55×10^{-3}	....	.....

The silver-ion concentration in protargol is about 10 times greater than in collargol solutions of the same concentration. I suppose that in Protargol the ionic silver will have the therapeutic effect, while in Collargol the metallic silver will have this action.

In Fig. 1 we represent our results in a graph. The abscissas represent the concentration of Protargol or Collargol, and the ordinates the silver-ion exponent p_{Ag}, that is, the negative logarithm of the silver-ion concentration.

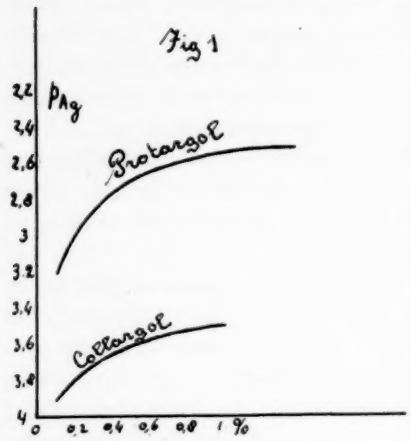


Fig. 1.

The "British Pharmaceutical Codex[1]" remarks: "The fact that solutions of silver proteinate are not precipitated by sodium chloride indicates that silver ions are not present, and any silver action can therefore result only after decomposition of the salt." From the above it is evident that this conclusion is not warranted; and as we will state in the next part, silver proteinate will react with halides, forming the corresponding silver salt. Due to the presence of the protecting colloids, these silver halides formed remain in colloidal solution, so that it gives the impression that no action occurs at all.

VI. In order to investigate whether all the silver in Protargol may be transformed into silver halides by treatment with halide solutions, we titrated solutions of silver proteinate with alkali-halides and measured the change of the silver-ion concentration during the titration by means of a silver electrode. Hence we made an application of the so-called "potentiometric titrations." I cannot enter into details about this method and must refer to preceding communications[2] concerning the performance of such a determination. Before I give the results of the determinations, I might refer to the variation in the silver-ion concentration in titrating an approximately 0.003 N silver-nitrate solution with 0.01 N solutions of alkali chloride, bromide and iodide respectively. In the graphs in Fig. 2 the left ordinate represents the values of "a" read on the slide wire, after the system was balanced and the right ordinate gives the corresponding silver-ion exponent p_{Ag}, *i. e.*, the negative logarithm of the silver-ion concentration, so

$$p_{Ag} = -\log (Ag^{\cdot}).$$

The abscissa gives the amount of reagent added. For the sake of clearness the abscissa is shifted in the titration with chloride 3 cc. to the right, and in titration with bromide 1 cc. to the right, so that the different curves cannot coincide.

In Fig. 2, the rise in potential is the greatest in titrating with iodide, as the silver iodide is the least soluble of the three silver halides; the jump is smaller in titrating with bromide and it is the smallest in the titration with chloride.

Now we proceeded to the titration of Protargol solutions in neutral and acid mediums. As the best results were obtained in the presence of sulphuric acid, I

[1] "British Pharmaceutical Codex," 1911; p. 148.

[2] Published in *Rec. Trav. Chim.* 1919 up-to-date, where reference is made to other literature.

give, in Fig. 3 only the curves obtained in the presence of this acid. Fifty cc. of a 1 per cent. Protargol solution were mixed with 5 cc. 4 *N* sulphuric acid and titrated with 0.01 *N* sodium chloride, 0.01 *N* potassium bromide, and 0.01 *N* potassium iodide respectively.

Figure 3.—Though the liquids remained perfectly clear during the titrations, it is evident from the variation of the silver-ion concentration that all the silver is transformed into the corresponding silver halide. In the titration with chloride the rise in the potential is not great. From this may be concluded that the solubility of the silver proteinate is a little greater than that of silver chloride. After the addition of the amount of chloride corresponding to the quantity of silver present in

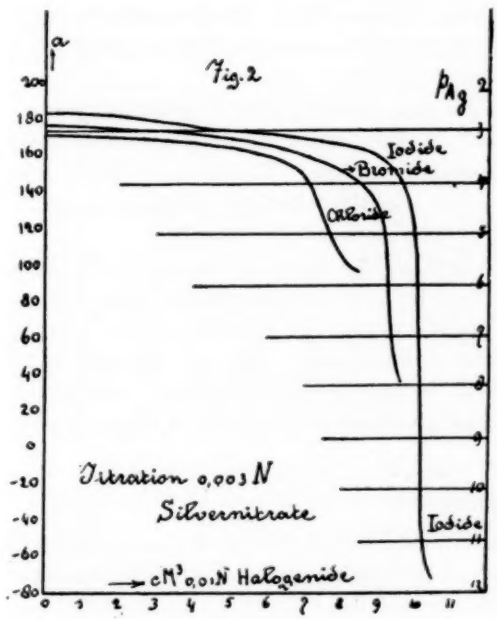


Fig. 2.

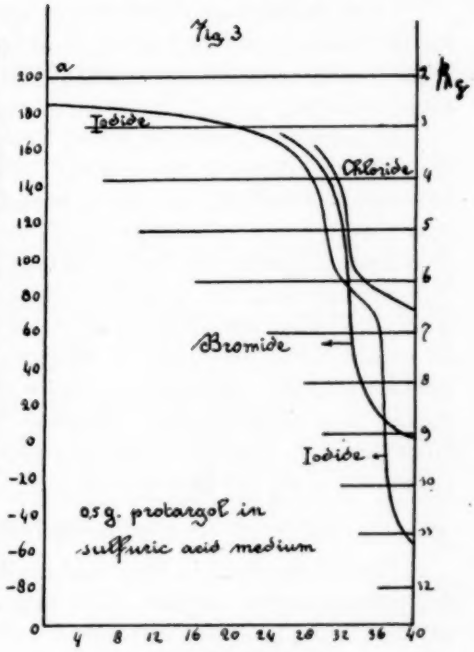


Fig. 3.

the protargol, all the silver is not completely transformed into silver chloride, but there is an equilibrium represented by the equation.

$$\text{Ag prot.} + \text{Cl}' \rightleftarrows \text{AgCl} + \text{prot}'.$$

In the presence of acid this equilibrium is shifted to the right.

Hence, we have at the equivalent point silver proteinate in the presence of a large excess of silver chloride. When an excess of chloride is added, all the silver is transformed into silver chloride.

In titrating with bromide, the rise in potential is greater than is the case with chloride, but it occurs at the same place. In the titration with iodide, two jumps occur, the first corresponding to that obtained with the two other halide solutions. At that point, all the silver of the Protargol is transformed into silver halide. We found that 0.5 Gm. Protargol bound 32.75 cc. 0.01 *N* halide solution, corresponding to a content of 7.08% silver.

The second rise in the titration with iodide occurs after the transformation of the silver chloride—present in the Protargol—into silver iodide.

$$AgCl + I' = AgCl + Cl'$$

We found that 0.5 Gm. Protargol took (36.6 − 32.75) = 3.85 cc. 0.01 *N* iodide solution for the transformation of the silver chloride in iodide. This corresponds to a content of 0.83% silver in the state of silver chloride. By means of this potentiometric titration we found a total silver content of 7.08 + 0.83 = 7.91%, and 0.83% silver as chloride. This agrees very well with the results found according to the usual method of analysis communicated above, by which we found a total silver content of 7.87% and 0.79% silver as silver chloride.

I wish to emphasize that we can apply here with great advantage the potentiometric titration, as it is possible to determine by one simple titration with a standardized iodide solution the total silver content and the amount of silver present as silver chloride.

In connection with the use of Protargol as a remedy, it is of great interest to state that solutions of this preparation have a good buffer value for silver ions between p_{Ag} 2.8 and 4.0, as can be read from the curves. Therefore, it is evident that the silver-ion concentration will vary but slightly, when the protargol is introduced into a liquid of the body that contains small amounts of chloride.

Summarizing the results—we stated that all the silver in Protargol can react with a halide, in which case it is transformed into the corresponding silver halide. In contradistinction to this, Collargol consists mainly of metallic silver, a small amount probably being present in the form of silver oxide; this we determined by means of a potentiometric titration with iodide in acid solution. Moreover, from the latter titration could be concluded that our preparation, Collargol, contained 5% silver as silver chloride.

BRIEF SUMMARY.

1. All the silver in Protargol can be titrated with iodide by the application of the potentiometric method. The first rise in potential occurs after transformation of the silver proteinate into silver iodide, the second after the transformation of silver chloride into silver iodide.

2. A Protargol solution has a good buffer value for silver ions between p_{Ag} from 2.8 to 4.0.

3. Collargol contains nearly all the silver in the metallic state; only a small part is present in the ionogenic form (oxide). The latter can be determined by means of a potentiometric titration with iodide; at the same time we find the silver present as silver chloride.

ABSTRACT OF DISCUSSION.

J. C. Munch: What chemical characteristic would most closely agree with the irritability of this type of compound? It is my understanding that silver-nitrate solution itself is no longer used because it is too irritant.

Dr. Kolthoff: You ask me why this can be used in medicine and why the silver nitrate cannot be used? I think that owing to the presence of the colloid in this case, most of the silver ions are adsorbed on the surface of the proteid. The silver-ion concentration is rather low and though you are working in a concentration of one, two, three or four per cent., you don't get increased ion concentration. It doesn't increase when you increase the concentration, or hardly increases, but when you have a solution of silver nitrate and you make a more concentrated solution, the silver-

ion concentration increases just the same as the concentration of the salt itself increases. Whereas, when you have the silver proteid the largest part of the silver ions are forming some chemical complex or colloidal complex with the proteids present, and so they don't irritate the tissues in the body.

H. B. Corbitt: You state that there is silver colloid there in the colloidal dispersion. In such a state I believe it could be carried to any part of the body, say, to the face, and might be deposited under the skin. Does the sunlight affect it? Do you know of any cases of argyria?

Dr. Kolthoff: When you take silver nitrate it is reduced in the body to metallic silver, and the metallic silver deposits in the cells just under the skin, but it is not sunlight which plays the rôle but only special characteristics of the cells of the skin that are doing that, because it is not only in the skin that you have metallic silver but also in other cells of the body. I am not quite sure where all these cells are because I am not a pharmacologist, only a chemist and pharmacist. The main part is deposited in the cells just under the skin.

A PHARMACOGNOSTIC AND CHEMICAL STUDY OF MA HUANG (EPHEDRA VULGARIS VAR. HELVETICA).

BY K. K. CHEN.*

I. INTRODUCTION.

In a preliminary report of experiments with Ma Huang (1) it was noted that the drug possessed actions very similar to those of adrenaline, and that these were due to an alkaloid which had been identified as Ephedrine. A more complete report of these experiments and of the results of administration of ephedrine to normal and diseased men has been published (2). It appears from the pharmacodynamic studies that ephedrine is of considerable value as a circulatory stimulant in surgical shock, as a bronchodilator in asthma, as a mydriatic, and as an apparently specific remedy in Addison's disease. Since ephedrine is effectively absorbed from the gastrointestinal tract, and since solutions of the alkaloid are very stable, it appears to be a drug of definite clinical value. Naturally the identification of the plant and alkaloid is of some importance.

II. HISTORY.

Ma Huang has been identified as *Ephedra vulgaris* var. *helvetica*, family *Gnetaceae* (3). In Chinese characters, *Ma* means "astringent" and *Huang* "yellow;" the former probably refers to taste and the latter to color after storage. It was tasted and placed by Emperor Shen Nung some 5100 years ago in the "medium class" (4). It entered many famous prescriptions, and appeared in "Pentsao Kang Mu," the Chinese Dispensatory written in 1596 A.D. (5). No scientific investigation was made until Nagai (6) isolated an alkaloid from it which he named ephedrine. Its empirical formula is $C_{10}H_{15}ON$; its chemical structure has been repeatedly studied (7) (8) (9) and is most probably phenyl -ol *1*-methyl *2*-methylamino *2*-ethane, $C_6H_5OH.CH.CH.CH_3.NHCH_3$.

III. GEOGRAPHICAL DISTRIBUTION.

The exact distribution of the plant requires an accurate survey. It has been reported that in China it is indigenous to the sea coast (3), to west Szechuan near

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Tachienlu (10), and to several districts of Kansu, Shensi, Honan, Shangtung and Kiangsu Provinces (5). In central Europe, the plant was known to have originated from the Orient, and the Mediterranean basin (11). The European variety is, however, not the same as the Asiatic for the alkaloid isolated and named pseudoephedrine by Merck (12) is isomeric but not identical with Ephedrine.

Fig. 1.—Ma Huang, Ephedra vulgaris, var. helvetica.

IV. DESCRIPTION OF THE PLANT.

Ephedra vulgaris var. helvetica is a low, dioecious, practically leafless shrub, 60–90 centimeters high (Fig. 1). The stem, green in color, is slender, erect, somewhat ribbed and channelled, 1.5 millimeters in diameter, and usually terminating in a sharp point. On the stem there are nodes, 4–6 centimeters apart, at which the leaves appear as whitish, triangular, scarious sheaths. Branching occasionally takes place at the nodes. The plant blossoms in the summer. It is sold by the native drug stores in the form of dried brownish green sticks, 1–1.5 centimeters long, known as Ma Huang.

V. HISTOLOGY OF THE STEM.

A transverse section (Fig. 2) made from the dried specimen shows that it is somewhat circular or elliptical in shape with ribbed edges. The epidermis (Ep.) consists of a single layer of cells, the radial diameter of each cell measuring 22–24μ and the tangential one 20–24μ. The outer wall is much thicker than the others, its cellulose layer being 4μ, while the cutinized layer is 6μ, in thickness. A cuticle covers the surface. At the apex of the ribs certain cells have their cutinized walls swollen including some cellulose forming trichone-like projections. The cytoplasm of all the epidermal cells appears to occupy a rectangular space. A number of stomata are found between these cells. The remaining cortical region is made of several layers of thin-walled parenchymatous cells (Par), polygonal in shape, varying from 14–36μ in diameter and containing chloroplasts and simple sugars which can be demonstrated microchemically. Their nuclei can be stained by safran and measure about 7μ in diameter. Here and there they are intermingled with air spaces (A) and islands of bast fibers (B). The latter are angular and thick-walled, and measure 14–20μ in diameter. The vascular bundles, ten in number, wedge-shaped with apex pointing to the center, belonging to the open, collateral type, are just next to these parenchyma cells. The phlœm consists of bast fibres, not much different from those in the outer region, phlœm parenchyma and cambium cells

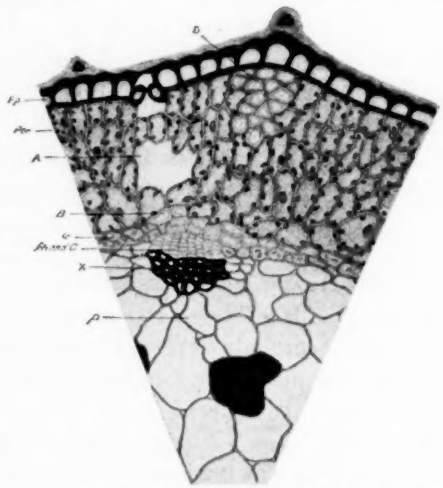

Fig. 2.—Transverse Section of the Stem of Ma Huang. Ep, Epidermis with a stoma. B, bast fibres. Par, parenchyma with chloroplasts. A, air space. Ph and C, phlœm parenchyma and fascicular cambium. Ic, interfascicular cambium with starch granules. X, xylem. P. pith.

(Ph and C) which are thin-walled and measure only about 6–8μ in diameter. The xylem (X) consists of thick-walled cells. Their radial diameter, 10–12μ, is greater than their tangential diameter, 7μ. The interfascicular cambium (Ic) joins the fascicular cambium to form a continuous ring. These cells as well as the neighboring parenchyma cells contain starch granules which can be stained blue with iodine solution. The cells of this portion of the cambium are larger than those in the fascicular cambium, being 12–16μ thick, 32μ wide. The center of the stem constitutes the pith (P), consisting of rather round, large, dead cells, measuring 70μ or more in diameter, and sometimes containing a homogeneous brown substance of unknown nature. Intercellular spaces are of frequent occurrence.

A longitudinal section of the stem (Fig. 3) shows the epidermis (Ep) as a layer of elongated cells, varying from 72 to 94μ in length. The bast fibres (B) are too long for microscopic measurement. Their ends are rather blunt. The chlorophyll-bearing parenchyma (Par.) looks very much like the spongy layer of a leaf. The cells in the phlœm parenchyma are longer than those in the cambium, being 100μ instead of 56μ. The xylem portion (X) consists of spiral (Sp.) and pitted (not shown) vessels, and tracheides (Tr) with bordered pits. Some of the tracheides are 286–300μ long. The shortest pith cells (P) measure 280μ in their longitudinal diameter.

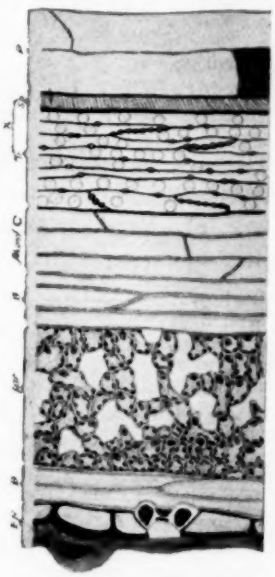

Fig. 3.—Longitudinal section of the stem of Ma Huang. Ep, Epidermis with a stoma. B, bast fibres. Par, parenchyma resembling spongy layer of a leaf. Ph and C, phloem parenchyma and fascicular cambium. Sp. spiral vessel. Tr, tracheides with bordered pits. X, xylem. P, pith.

VI. EPHEDRINE, THE ALKALOID OF MA HUANG.

(a) *Isolation*.—This active principle can easily be isolated by means of immiscible solvents. The most satisfactory procedure was as follows: The drug was ground to No. 40 powder and percolated with 80% alcohol until the percolate was colorless. The percolate was distilled on a water-bath under diminished pressure at about 52° C. until a syrupy fluid was obtained. The latter was diluted with water, rendered alkaline with ammonium hydroxide, and filtered. As it was found that the alkaloid is soluble in water, the filtrate was shaken with chloroform twice, while the residue on the filter was extracted twice with the same solvent on a water-bath connected to a reflux condenser for an hour or more. The combined chloroform extract was subjected to distillation until a small volume was obtained, and then left to spontaneous evaporation. The greenish, fragrant gelatinous residue was dissolved in a small volume of hot water and treated with dilute hydrochloric or sulphuric acid until exactly neutral to litmus paper. After evaporation on the water-bath, the residual alkaloidal salt was dissolved in a minimum volume of absolute alcohol and crystallized out by chilling in a mixture of salt and ice, ether being added to hasten and complete the crystallization. It was purified by recrystallization from alcohol three times. The alkaloid itself can be regenerated by making the salt solution definitely alkaline with ammonium hydroxide and shaking and

crystallizing out from chloroform. It appears as white rosette crystals easily broken up into coarse needles, its hydrochloride as fine white needles, and its sulphate as white, plate-like, rhombic crystals. We tried to shorten the process of preparation by mixing the sticks sold on the market with slaked lime and extracting with alcohol on the water-bath connected to a reflux condenser to save the trouble of powdering and percolation, but we found that the yield of alkaloid was less satisfactory.

(b) *Identification.*—The physical constants of the base and its salts we have found to be as follows:

	Melting point.	Specific rotation.
Ephedrine	210° C.	–
Ephedrine HCl	214° C.	$[\alpha]_D^{25} - 35°$ (in water).
Ephedrine H_2SO_4	242° C.	

The melting points of the base and its hydrochloride are in perfect agreement with the figures obtained by Nagai (13).

(c) *Reactions towards alkaloidal Reagents.*—The results are shown below and need no explanation:

Reagent.	*Result.*
Mayer's	Cloudy on standing
Wagner's	Orange precipitate
Phosphomolybdic acid	Greenish yellow heavy precipitate, blue on standing
Phosphotungstic acid	Heavy white precipitate
Erdmann's	Yellow ring below, pink ring above and smoky pink layer on top
Concentrated H_2SO_4	Same as Erdmann's
Concentrated $H_2SO_4 + K_2Cr_2O_7$	Bluish green, turning brown
Tannic acid	No color change or precipitate
Picric acid	No color change or precipitate
Concentrated HNO_3	No color change or precipitate
$FeCl_3$	No color change or precipitate.

(d) *Assay.*—This was performed volumetrically by following the method of Assay of Belladonna Root given in U. S. P. IX (14). In the first step we used a mixture of chloroform, 1 volume, and ether, 3 volumes, and finally employed methyl red as the indicator instead of cochineal. Each cubic centimeter of $N/10$ H_2SO_4 used corresponds to 16.513 milligrams of ephedrine. From three different samples of crude drug, we obtained the following figures:

Sample 1	Ephedrine 0.01858% average of 3 determinations
Sample 2	Ephedrine 0.07214% average of 3 determinations
Sample 3	Ephedrine 0.09082% average of 3 determinations

The duplicate determinations checked very well. It appears that the content of the alkaloid is small and varies considerably.

VII. DETERMINATION OF MOISTURE, VOLATILE SUBSTANCE AND ASH CONTENTS.

Four grams of No. 60 powder were weighed in a tared crucible, previously heated to constant weight, and placed in a desiccator until there was no more loss

of weight. The difference is the amount of moisture in the powder. The contents were then put on a water-bath until constant weight was reached. This second difference represents the amount of volatile substances. The powder was then incinerated in an electric muffle furnace and the weight of ash determined. The following data were obtained from different samples of the crude drug:

Sample no.	Determination no.	Moisture in %. Individual.	Moisture in %. Average.	Volatile substances in %. Individual.	Volatile substances in %. Average.	Ash in %. Individual.	Ash in %. Average.
	1	4.607	.....	1.750	.....	7.350	.....
I	2	4.570	4.569	1.815	1.796	7.295	8.315
	3	4.530	.....	1.825	.....	7.300	.....
	1	.....	.....	.....	.....	8.397	.....
II	2	.....	.....	.....	.....	8.374	8.399
	3	.....	.....	.....	.....	8.427	.....
	1	.....	.....	.....	.....	8.280	.....
III	2	.....	.....	.....	.....	8.378	8.352
	3	.....	.....	.....	.....	8.399	.....
IV	1	.....	.....	.....	.....	8.350	8.350

The moisture and volatile substances vary with climate. In Peking where the weather is dry, especially in winter, one would look for a low percentage, while in Shanghai where the weather is damp one would expect it to be higher. The percentage of ash seems to be more constant, about 8.5%.

VIII. ANALYSIS OF ASH.

Besides the water soluble, acid soluble (in 10% hydrochloric acid) and insoluble portions, we have analyzed the individual common elements of the ash. For sampling, 10 grams of the powdered drug were ignited, and the ash was treated with concentrated nitric acid to precipitate silicates. After evaporation to dryness the residue was dissolved in dilute nitric acid and made up to 250 cc. Aliquot portions were taken for investigation of these elements. Chlorine was determined by Volhard's method, sulphur by precipitation as barium sulphate, phosphorus colorimetrically by Briggs' modification of Bell-Doisy's method (15), calcium by precipitation with ammonium oxalate ignited and weighed as calcium oxide, potassium by precipitation with platinic chloride, weighed as potassium chloroplatinate, and sodium by the difference calculated from the total weight of potassium and sodium chloride previously determined. Duplicates were made from separate ash samples. The results are shown in the following table:

Analysis for	Determination no.	Individual % of ash.	Average % of ash.
	1	21.600	.....
H_2O soluble ash	2	18.610	20.260
	3	20.580	.....
	1	60.310	.....
HCl soluble ash	2	63.090	60.960
	3	59.470	.....
	1	18.100	.....
Insoluble ash	2	18.290	18.780
	3	19.950	.....
	1	0.257	.....
Chlorine	2	0.254	0.271
	3	0.302	.....
	1	1.643	.....

Analysis for	Determination no.	Individual % of ash.	Average % of ash.
Sulphur	2	1.602	1.608
	3	1.578	.....
	1	2.047	.....
Phosphorus	2	2.023	2.022
	3	1.995	.....
	1	30.180	.....
Calcium	2	31.190	30.500
	3	30.120	.....
	1	3.129	.....
Potassium	2	3.399	3.456
	3	3.840	.....
	1	9.055	.....
Sodium	2	8.725	8.886
	3	8.877	.....

Iron and manganese were also present in small amount, but were not determined quantitatively.

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(2) K. K. Chen and Carl F. Schmidt, *J. Pharmacol. Exp. Therap.*, 24, 339 (1924).

(3) Botanical Nomenclature, *Commercial Press*, Shanghai, p. 1004 (1917).

(4) Emperor Shen Nung, 3217–3077 B.C., father of Chinese Agriculture, tasted many medicinal plants. It is believed that he wrote "Pentsao," containing 360 drugs, divided into "superior," "medium" and "inferior" classes.

(5) "Pentsao Kang Mu," the Chinese Dispensatory, is a revision of "Pentsao" by Li Shih Cheng in 1596 A.D., greatly enlarged, containing 1871 drugs under 62 orders and 16 classes, in 52 Chapters.

(6) Nagai, *Pharm. Zeit.*, 32, 700 (1887).

(7) A. Ladenburg and C. Oelschagel, *Ber.*, 22, 1823 (1889).

(8) P. Rabe, *Ber.*, 44, 824 (1911).

(9) E. Schmidt, *Arch. Pharm.*, 253, 52 (1915).

(10) F. B. Forbes and W. B. Hemsley, "Index Floræ sinensis," 2, 539 (1889–1902).

(11) A. Engler and K. Prantl, "Die natürlichen Pflanzenfamilien," 2, I, 118 (1889).

(12) *Merck's Ber.*, 13 (1893).

(13) I. Guareschi and H. Kunzkranse, "Einfübrung in das Studium der Alkaloide," 480 (1896).

(14) "The Pharmacopœia of the United States of America," 73 (1916).

(15) A. P. Briggs, *Jour. Biol. Chem.*, 53, 13 (1922).

JOHN SIMON GUGGENHEIM MEMORIAL FOUNDATION.

Former U. S. Senator Simon Guggenheim, of Colorado, has made a preliminary gift of $3,000,000 for establishing a fund which will support fellowships for research. The provisions are somewhat along the lines of the Rhodes scholarships, however, intended for men and women who have demonstrated creative power in science and the arts. The stipend will be approximately $2500 a year, and it is expected that after the first year between 40 and 50 scholarships will be maintained. The appointees must have shown marked ability in their special fields. Professors on sabbatical leave, or individuals holding other fellowships, will be eligible, as well as other candidates. The Secretary of the Foundation is Henry Allen Moe, and may be addressed at 120 Broadway, New York.

THE ANATOMY AND BOTANICAL POSITION OF MIRÉ.*

BY HEBER W. YOUNGKEN.

Miré (pronounced Meé-ray), the plant whose structural characteristics and identity form the theme of the subject matter of this investigation, is the native aboriginal name of a shrub, parts of which members of the recent Mulford Biological Exploration party, under the direction of Dr. H. H. Rusby, brought back with them from Central Bolivia. Rusby (JOUR. A. PH. A., Vol. 13, p. 101) noticed that the Indians of that country employed the plant as a muscular paralysant and remedy for cutaneous parasites. Since it gave promise of being a valuable addition to the present list of the world's medicaments, Dr. Rusby, upon his return, sent

Fig. 1.—Leafy branch of Miré, a Central Bolivian shrub belonging to the genus *Brunfelsia* (Fam. *Solanaceæ*.) (× 1/2).

Fig. 2.—Aerial stems of Miré (× 1/2).

me some material with a view to determine its anatomical characteristics and, if possible, its botanical relationship.

The material received and described herein represented about 3 pounds of dried aerial stems and rhizomes with few rootlets, a specimen of rhizome with rootlets and a leafy aerial stem (Fig. 1), the latter collected August 10, 1921 by Dr. O. E. White in the vicinity of Huachi, Bolivia, at an altitude of 1800 feet.

DESCRIPTION OF RHIZOMES AND ROOTS.

Rhizomes of horizontal or oblique growth, occurring in cylindrical to subcylindrical segments, occasionally tortuous and furcately branched, up to 32 cm. in length and from 1.5 to 2 cm. in thickness. Externally, varying from light brown and longitudinally striate to reddish brown, longitudinally wrinkled and transversely fissured to reddish brown; warty, with abraded cork in very

* Scientific Section A. PH. A., Buffalo meeting, 1924.

old portions, with oval to circular stem scars on upper or lateral surfaces of nodes and a few slender, filiform, wiry rootlets of brown color, or circular scars of these, on both lower and lateral surfaces; internally with very thin bark, broad, dense, yellowish brown wood and narrow, pale yellow pith; fracture of bark short-fibrous and of wood tough, uneven and splintery; odor very slightly aromatic upon burning, pop-corn like; taste sweetish, followed by a tingling sensation and, later, by a sensation of numbness.

HISTOLOGY OF RHIZOME.

The rhizome of Miré (Fig. 2) presents the following microscopic features passing from periphery toward the center:

1. A cork zone (*k*) composed of several rows of cork cells having lignified walls. These are rectangular in transverse view and polygonal in longitudinal section. Certain of the cork cells show most of their thickening on the inner tangential walls.
2. A cork cambium of more or less collapsed meristematic cells.
3. A cortex (*co*) of somewhat tangentially elongated cortical parenchyma cells. Most of these cells are filled with starch grains, but scattered through many parts of this region are cells containing rosette aggregates of calcium oxalate. Stone cells occur in the outer region of this part of the bark but are not evident in all sections. They are frequently oblong in longitudinal sections and many occur singly or in groups.
4. A narrow pericycle composed mainly of starch-containing parenchyma within which region is a discontinuous arc of narrow, slightly lignified sclerenchyma fibers (*scl*^{2}).
5. A phloem (*ph*) occupying up to one-third the width of the bark and consisting of numerous phloem patches separated by phloem medullary-rays which are mostly 1-cell in width. An interrupted zone of strongly lignified bast fibers (*bf*) occurs in the protophloem composed of small fiber groups and isolated fibers.
6. A cambium (*c*) forming an irregular wavy circle of collapsed meristematic cells which readily separate from the wood in sectioning.
7. A broad xylem composed of many narrow xylem wedges separated by lignified xylem medullary-rays (*mr*), the latter mostly 1-cell in width and containing abundant starch. The xylem wedges contain numerous thick-walled, greatly lignified wood fibers (*wf*) with oblique pits and relatively few porous and spiral tracheae, the latter most evident in the protoxylem region.
8. An inner cambium (c^2) of meristematic cells.
9. A narrow internal phloem (*ip*) composed of soft bast patches separated by narrow medullary-rays with non-lignified walls. A few narrow sclerenchyma fibers (*scl*^{1}) accompany the soft bast on its inner face.
10. A central pith (*m*) of rounded to polygonal parenchyma cells, most of which are loaded with starch while some contain a rosette aggregate of calcium oxalate. Scattered about in this region are numerous stone cells with broad lignified and porous walls and narow lumina. These appear irregularly-rounded to polygonal in transverse section and oblong to irregularly polygonal in longitudinal section. The starch grains (see Fig. 7) found in the parenchyma of the cortex pericycle and pith vary from simple, spheroidal or oval to 2-, 3-, or 4-compound, the larger single grains measuring from 6μ to 15.44μ in diameter or in length.

The hilum in many instances is circular but may be a triangular or linear cleft. Lamellæ are indistinct.

The rosette aggregates, found in the same regions, measured from 46μ to 115.8μ in diameter. The wood fibers are frequently irregularly wavy-walled and undulate, show oblique pits and short to long pointed or blunt ends. The tendency of these fibers to become curved toward the ends is common. Tracheae and tracheids with distinct and indistinct bordered pits occur in the xylem. The wood parenchyma is scantily developed.

Fig. 3.—Transverse section through a representative portion of Miré rhizome showing cork (k), cortex (co), rosette aggregate crystals (r), sclerenchyma fibers (scl¹) in medullary sheath, in pericycle (scl²), phloem (ph), bast fibers in protophloem (bf), cambium (c), intraxylary phloem (ip), medullary-rays(mr); wood fibers (wf) and tracheae (tr) of xylem; medulla (m), and stone cells (s) (*highly magnified*).

DESCRIPTION OF AERIAL STEM.

In simple or furcately-branched cylindrical segments (Fig. 3) up to 30 cm. long and from 1 mm. to 15 mm. in thickness; externally light brown and covered here and there with grayish green foliaceous lichens having blackish apothecia, longitudinally striate in younger parts to irregularly longitudinally wrinkled with numerous transverse lenticels in older portions, with prominent nodes, many of which exhibit circular, depressed stem scars, others conical buds; fracture of bark short-fibrous, of wood tough, splintery-fibrous; externally—bark thin, brownish and readily separable from broad yellowish brown wood; pith narrow, pale yellowish to light brown; odor and taste similar to rhizome.

HISTOLOGY OF AERIAL STEM.

Sections through the aerial stem exhibit the following structural characteristics, passing from periphery toward the center:

1. A cork of several rows of cork cells similar in character to those noted in the rhizome.
2. A phellogen of collapsed meristematic cells.
3. A broad cortex of tangentially elongated cortical parenchyma cells, some of which are filled with starch grains while many others contain a rosette aggregate of calcium oxalate. Stone cells with greatly lignified walls occur in the outer and inner portions of many though not all of the sections through this region

examined. They occur singly or in small groups and are tangentially elongated, as viewed in transverse sections.

4. A pericycle containing an interrupted circle of narrow sclerenchyma fibers, arranged singly and in groups, whose walls vary in extent of lignification, in sections treated with phloroglucin and hydrochloric acid.

5. A narrow phloem composed of radially arranged soft bast arms separated by non-lignified medullary-rays 1 cell in width.

6. A cambium forming an irregular wavy circle of meristematic cells.

7. A broad radiate and porous xylem of many narrow xylem wedges, composed of strongly lignified wood fibers, interspersed with fewer tracheae and tracheids and very few wood parenchyma cells. The xylem medullary-rays separating the wood wedges have lignified porous walls and contain starch. The tracheal elements appear more abundant than in the rhizome of equal age, have chiefly distinct and indistinct bordered pits and oblique to transverse, porous septa.

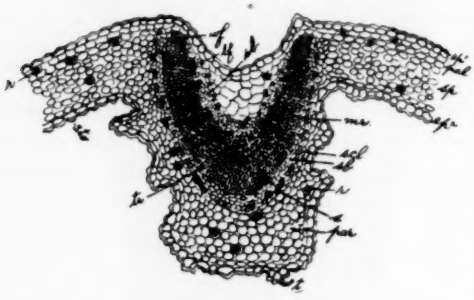

Fig. 4.—Transverse section of representative portion of Miré lamina including midrib, showing upper epidermis with striated cuticle (ep^1), palisade parenchyma (pal), spongy parenchyma (sp), lower epidermis (ep^2) with stomata (sto), rosette aggregates of calcium oxalate (r), group of sclerenchyma fibers (scl) and stone cell (s) in pericycle, parenchyma of midrib (par), stalk of glandular hair (t), medulary ray (mr), and wood fibers (wf), bast fibers (bf), tracheae (tr) and soft bast (sb) of bicollateral fibrovascular bundles (*magnified*).

8. An inner cambium of meristematic cells.

9. A narrow intraxylary phloem composed of soft bast. On the inner face of the soft bast, in what may be termed the medullary-sheath, occur narrow, highly lignified sclerenchyma fibers arranged singly or in small groups.

10. A broad central pith of rounded to slightly polygonal parenchyma cells most of which are filled with starch, while many contain a large rosette aggregate crystal. Polygonal to irregularly rounded-polygonal stone cells with greatly lignified walls and small lumen are scattered singly or in groups within this region.

DESCRIPTION OF LEAVES.

The leaves of Miré (see Fig. 1) are simple, alternate, petiolate, exstipulate, oblong-lanceolate to elliptic-oblong, glabrous on both surfaces, subcoriaceous, with pinnate-reticulate venation, entire or nearly entire margin, acute to acuminate apex and attenuate base. Their color when dried is grayish green on upper surface and brownish green on lower surface. The upper surface of the lamina is frequently spotted with emerald-green lichens, some possessing black apothecia. The leaves examined were up to 18 cm. in length and up to 5.8 cm. in width. The petioles were up to 8 mm. long. The midrib is concave on the upper and convex-crenate on the lower surface.

HISTOLOGY OF LEAF.

The lamina of the Miré leaf is dorsoventral in development. Transverse sections of (Fig. 4) this part outside of the midrib exhibit (1) an upper epidermis (ep^1)

devoid of stomata, the outer walls of which are wavy and possess a thick-striated cuticle, (2) a zone of one to two layers of tangentially elongated to irregularly cubical-shaped, compactly arranged palisade cells (*pal*) some of which contain a rosette aggregate crystal, of calcium oxalate (*r*), (3) a broad zone of somewhat loosely arranged spongy parenchyma, many of the cells of which possess a rosette aggregate crystal, (4) a lower epidermis containing numerous stomata, and whose outer cell walls are wavy and with thick cuticle.

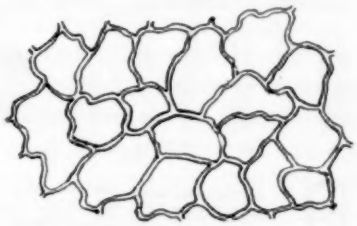

Fig. 5.—Upper epidermis of Miré in surface view *greatly* (*magnified*).

Surface sections of the upper epidermis (Fig. 5) show that the vertical walls of the upper epidermis cells are curvilinear except over the veins where they are rectilinear and the cells rectangular in shape. Surface sections of the lower epidermis (Fig. 6) show regular epidermal cells (*e*) with curvilinear vertical walls and numerous stomata (*s*), each of which is surrounded by a pair of subsidiary cells (*n*) of equal or unequal size and paralleled to the stomatal orifice.

Transverse sections through the midrib show that it is notched above and deeply convex below with several protuberances and sinuses. The epidermal cells over both surfaces exhibit a thick cuticle and wavy outer walls. Bi-collateral fibrovascular bundles occupy a crescentic area within the midrib, with ends of the crescent facing toward the upper epidermis. These show dense radiate xylem wedges separated by medullary-rays 1 cell in width. The upper soft bast zone is flanked on its outer face by a discontinuous arc of narrow, thick-walled sclerenchyma fibers while the lower soft bast zone is accompanied by an outer discontinuous arc of often densely arranged pericyclic fibers, with an occasional stone cell. Glandular hairs with a short, curved somewhat appressed stalk 2 to 4 cells in length and an ellipsoidal to saucer-shaped peltate head occur on the epidermis of the midrib. Parenchyma cells, some of which contain a rosette aggregate crystal of calcium oxalate, occur between the bundle zone and the epidermises. These crystals measured up to 54μ in diameter.

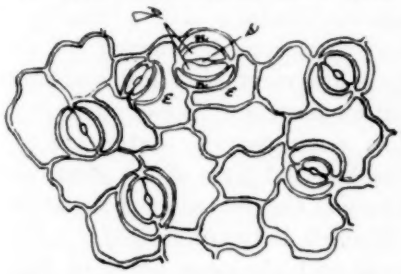

Fig. 6.—Lower epidermis of Miré in surface view. Note the stomata with neighboring cells (n) parallel to stomatal orifice (s); guard cells (g) and ordinary epidermal cells (e) (*greatly magnified*).

BOTANICAL POSITION OF MIRÉ.

The inability of the collectors of this plant to secure either flowers or fruits of this species, due to the season of the year when collected, obliged me to resort to pharmacognic methods in an attempt to establish its kinship. The presence in the axis and leaves of intraxylary soft bast accompanied on its inner face by sclerenchyma fibers, the scantily developed wood parenchyma, the presence of isolated groups of sclerenchyma fibers in the pericycle, tracheae with bordered pits, the absence of bast fibers in the secondary phloem, the narrow medullary-rays, and the absence of special internal secretory organs, all these together indicate that the plant is one of the *Solanaceæ*.

The occurrence of an occasional stone cell among the pericyclic fibers (as first noted by the writer in the midrib) the presence among certain of the cork cells of thickened inner tangential walls, and the occurrence of scattered stone cells in the pith are anatomically characteristic of several species of *Brunfelsia* as pointed out by Fedde (*Verg. Anat. d. S., Diss. Breslau*, 1896). These very structures, present in the Miré material examined, together with the other Solanaceous features heretofore indicated places Miré in the genus *Brunfelsia*.

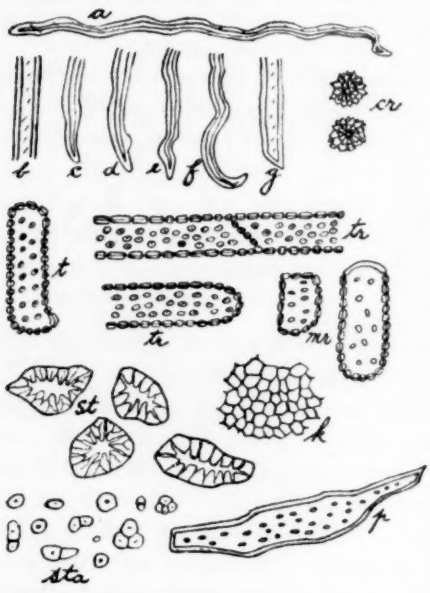

Fig. 7.—Histological elements found in the axis of Miré. Sclerenchyma fiber (a); median portion of sclerenchyma fiber (b); ends of sclerenchyma fibers (c, d, e, f, g); tracheid with bordered pores (t); tracheae (tr); medullary-ray-cells (mr); stone cells from pith (st); cork tissue (k); pitted vessel (p) and starch grains (sta) (*highly magnified*).

While comparing the Miré material with various mounted species of *Brunfelsia* in the gray Herbarium of Harvard University, I came upon a mounted herbarium specimen labeled "*Brunfelsia hydrangaeformis* (Pohl) Benth"[1] which was collected at Uchimachi, Coroico, Bolivia, July 20, 1894 by Miguel Bang and distributed by Drs. Britton and Rusby. This specimen agreed in every respect macroscopically with the plant which Pohl figured and described in his *Plantarum Brasille*, plate 7, 1827 and which de Candolle also described in *Prodromus*, part X, 1846. The leaves and stem of this plant appeared so strikingly like similar parts of Miré that I decided to make a microscopic comparison. Through the kindness of Dr. Hirschy of the Gray herbarium, I obtained for this purpose a fragment of a leaf and short segment of a stem. These, when compared histologically with Miré, showed many close resemblances. Later, through the kindness of Dr. Rusby, I obtained an entire leaf and piece of the stem from another herbarium sheet in the New York Botanical Garden which was labeled "*Brunfelsia hydrangaeformis* Pohl. collected by Weddell, in Brazil, in 1847." After a careful microscopic comparison of this material with the same parts of Miré, I find both exhibit a striking similarity of structure.

Department of Materia Medica,
Massachusetts College of Pharmacy,
August 19, 1924.

[1] Dr. H. H. Rusby has accepted the author's determination of the botanical origin of Miré as *Brunfelsia hydrangaeformis* (Pohl) after a comparison of it with a series of specimens collected by himself and others.

CASTELA NICHOLSONI, HOOKER, SIMARUBACEAE. BOTANY, PHARMACOLOGY, AND THERAPY.*[1]

BY ALBERT SCHNEIDER, M.D.

These investigations, as far as planned for the time, were completed during the early part of 1923, but the laboratory notes and correspondence, inclusive of the drawings, as well as most of the text matter, were destroyed in the Berkeley fire of September 17th, 1923. These circumstances will account for the delay in submitting the report. Furthermore, much of the correspondence and pharmacologic laboratory data could not be repeated or duplicated and are here summarized largely from memory. The drawings by my daughter have been remade, but three excellent photographic productions showing the morphology of the leaves and stems of the drug plant, furnished by Mr. Crosbie (through the courtesy of H. Engelhardt) of the firm of Sharp and Dohme, intended as a contribution to the report, were also destroyed in the fire mentioned and could not be duplicated.

The interest in *Castela Nicholsoni*, known as *Chaparro amargosa* and as Mexican bitter bush or simply as bitter bush, and also goat bush, was awakened through the published articles by the Nixons of Texas, in which they report on its value in the treatment of amebic dysentery. The plant has long been known to the natives of Mexico who considered it almost infallible in the treatment of dysentery. It is known that the army of Zachary Taylor, during the Mexican war, acting on the reports of the Mexican Indians, also used this drug against dysentery, with great success. Putegnat reports a case of malaria which was treated successfully by an infusion of Chaparro. The Nixons of Gonzales, Texas, were, however, the first to give the drug serious attention and to try it out therapeutically in many cases of amebic dysentery.

Mr. Nixon of Honda, Texas, furnished 100 pounds of the crude drug (stems and leaves) of recent growth. The preliminary investigations with this material were begun in the laboratories of the School of Pharmacy of the University of Nebraska. Miss Naomi Zimmermann of the Department of Chemistry began the chemical investigation of the drug but soon abandoned the undertaking for other work. It was her opinion that the active constituent was glucosidal in nature. Mr. Bukey, of the School of Pharmacy, verified the work by Putegnat as to the chemical constituents present but his results cannot be given as his report was destroyed in the fire mentioned. Miss Gretchen Sprecher, a student in the School of Pharmacy of the University of Nebraska, made a comparative study of the toxicity of the purified (detannated and degummed) solid (dry) extract of Chaparro and of emetin hydrochloride, on frogs, and found that the latter was about 20 times more toxic than the former, results which were found to be approximately correct according to subsequent tests. The final investigations, as herein recorded, were carried out in the laboratories of the North Pacific College of Oregon, Portland. The report hereby follows.

Botany of *Castella Nicholsoni* Hook, Simarubaceae.—A genus of three or four known species mostly natives of the Antilles, one of which (namely the one herein

* Scientific Section A. PH. A., Buffalo meeting, 1924.

[1] The expenses of this investigation have been supported in part by a grant from the Research Fund of the AMERICAN PHARMACEUTICAL ASSOCIATION.

described) is found on the coast of Texas and in northern Mexico. They grow in arid soils.

Flowers by abortion polygamo-diœcious, small, solitary or somewhat fascicled in the axils of the leaves, subsessile, saffron colored. The calyx is small, four ovate to triangular sepals united at the base, deciduous. Petals four, oval, concave, much larger than the sepals, hypogynous, imbricate in estivation, deciduous. Stamens 8, alternate and opposite the petals into the base of a very short gynophore or hypogynous disk, filaments subulate, anthers cordate-ovate, fixed near the base, extrorse, two-celled, longitudinally dehiscent. Pistil wanting or abortive in the sterile flowers; in the fertile, seated on the very short gynophore, of four carpels united only at the axis; ovary deeply four-lobed, four-celled, the cells opposite the petals; styles distinct or united at the base, acute, revolute, stigmatose down the inner face. Ovule solitary and pendulous in each cell, anatropous.

Fruit of four distinct spreading substipitate drupes, or by abortion fewer; the rugose or pitted and compressed endocarp at length two-valved after the fleshy exocarp dries up. Seed solitary, conformed to the cell, obovate, pendulous, anatropous, with the micropyle a little produced, testa membranaceous. Embryo large in thin fleshy albumen. Cotyledons broad and flat, foliaceous, caulicle short, superior.

Low, very woody shrubs with sharply spinescent branches also bearing spines in the axils of the small, oblong-ovate, thick rigid, entire, alternate, subsessile leaves. The leaves are smooth shining above, silvery-canescent underneath, falling away easily on drying. Stipules none. Numerous trichomes; and stomata few on lower surface, wanting on upper surface. (See figures.)

Morphology and Histology.—The plant reveals some interesting morphological adaptations to soil and climate. It is a dry soil (arid) plant found in regions with a minimum of rainfall (annual precipitation of $^1/_2$ to $1^1/_2$ inches) but with a fairly high nocturnal atmospheric moisture. The leaves are small, comparatively few in number, and the photosynthetic processes take place largely in the chlorophyll-bearing parenchyma of the younger branches. The branches are provided with remarkable water pores, and the vascular conducting tissue of the woody center is associated with a water-storing tissue. Each water pore consists of two parts. The outer crater-like portion receives the water which condenses (in the night) upon the greatly thickened cuticle of the epidermis. This moisture condensation is due to the rapid loss of heat *via* the trichomes and the greatly thickened cuticle, as soon as the sun has set. The guard cells now allow the condensed moisture to pass into and completely fill the second chamber or reservoir. The younger branches, as well as the lower surface of the leaves, contain numerous rather long and twisted single-celled trichomes, which also have greatly thickened walls (the cell-lumen being almost completely occluded). The heat irradiation of the trichomes is further increased by the numerous minute warty prominences of the cuticle. The trichomes thus play an important part in the surface precipitation as well as holding or storing (temporarily) of the the night air moisture. As is known, the thalli of crustose lichens are hygroscopic, readily taking up atmosphere moisture, and no doubt the abundant deposit of these plants upon the older stems and branches assists in the precipitation of atmospheric moisture for the use of both symbionts. In other words, the lichen deposits of the older branches in a measure take the place of the water pores of the younger branches.

The comparatively small volume of water which the plant can accumulate and store during the night is again used during the day. The plant probably would not survive in a soil area of equal paucity of moisture precipitation and less atmospheric moisture. Thus it probably would not thrive in the more inland arid regions of Mexico, Arizona and New Mexico, where the cactus with its much more highly developed water storing tissue can tide over variably prolonged periods of little night moisture. Castela is remarkably adapted to the rather limited coastal areas of little or no rain and considerable night moisture. Whether or not this plant would thrive in the sandy, gravelly soil of those regions having a more abundant rainfall and also considerable night atmosphere moisture, as southern California, has not been determined. Nor are there any accurate data as to the temperature ranges of this plant. For the time being there need be no concern as to the supply. There is also considerable uncertainty as to the exact geographic range of *Castela Nicholsoni* and as to its morphologic variation in different geographic areas.

The woody nature of the plant, the extremely bitter taste, and the abundant thorns and needle-like branch termini, protect it against herbivorous animals generally. Furthermore, the aridity of the countries in which Castela exists, greatly reduces the competitive struggle.

The lower surface of the leaves, and to a lesser degree also the stems, contain a small fungus (rust-like) which appears to find lodging among the trichomes. Whether or not this parasite contains any toxic or otherwise therapeutically objectionable substances has not been ascertained.

The dried shrub is very annoying to handle because of the thorns and sharp-pointed terminal branches. It is very hard and woody and can best be broken in a larger mill very coarsely set. The Nixons emphatically urge the use of the "tendrils" (old, now obsolete term for younger branches) for medicinal use, which advice should be heeded for reasons indicated above.

Chemistry of Castela.—The usual reagents gave no indication of the presence of alkaloids. Fehling's solution gave a marked reaction for invert sugar. Charring some of the extract on platinum first developed the odor of burning caramel, ending with an odor of creosote. Shaking with chloroform gives rise to an emulsion which endures for many hours. Apparently this represents a colloidal phase with the mucilaginous substance so abundantly present in the leaf hypoderm that the ultramicroscopic examination of the aqueous infusion reveals abundant particles manifesting the characteristic Brownian motion, which colloidal particles evidently belong to the mucilaginous cell contents.

Calcium oxalate is abundantly present in the leaves and also in the stem parenchyma, occurring in the form of prismatic crystals and some aggregates. Chlorophyll is abundantly present in the leaf and in the younger branches. The total ash of the stems is 7.4 per cent. according to Bukey. Starch is sparingly present in the stems, more abundant in the root system. Granules small, simple to compound. A small amount of oil is present.

According to Bosman, Castela contains a glucoside to which he gave the name *castelin*, and to the hydrolization product of the glucoside he applied the name *castelagenin*. Castelin can be purified by repeated cyrstallization from water, from which it separates in long, white needles and has a melting point of 205° C. It dissolves in 85 parts of water at room temperature, and in 25 parts of water at

100° C. It is more soluble in ethyl alcohol and in cold concentrated hydrochloric acid, and gives a deep violet coloration with concentrated sulphuric acid. The anhydrous castelin is highly hygroscopic, taking up 8 per cent. of its weight of water on exposure to air for an hour. It has the formula $C_{15}H_{22}O_8 + 3H_2O$, and is dextrorotatory (+62.9°) in aqueous solution.

Castelin is readily hydrolyzed by dilute acids and alkalies, a 20 per cent. solution of hydrochloric acid being the most satisfactory hydrolizing agent. The yield of castelagenin is rather low, barely exceeding 20 per cent. Castelagenin is readily soluble in boiling glacial acetic acid, from which it crystallizes in a pure condition. It is insoluble in chloroform, ether or acetone, but is freely soluble in warm methyl or ethyl alcohol. It has a melting point of 240–241° C., and gives no coloration with concentrated sulphuric acid. It is soluble in cold phenol and dextrorotatory (+59°), and its reaction with sodium hydroxide and sodium carbonate indicate that it is lactonic in nature. On oxidation with 30 per cent. nitric acid at 150° C. it yields a minute quantity of crystalline acid (melting point 128–129° C.), which is somewhat soluble in ether and gives the fluorescin reaction and appears to be a dicarboxylic acid.

The bitter principle castelamarin can be deposited out from warm alcohol, appearing in the form of aggregates of slender needles (60 per cent. alcohol with a few drops of sodic hydrates solution, and precipitating with dilute hydrochloric acid). Bosman suggests that the bitter principle is closely related to the glucoside castelin, differing from it chemically by only two atoms of hydrogen. Castelamarin is exceedingly bitter and gives a deep blue coloration with concentrated sulphuric acid which fades to a dirty brown after a few minutes.

Since Putegnat (1883) claims to have isolated a bitter principle (amorphous) to which he applied the name "amargosin," according to the rule of priority in nomenclature, that name would be retained rather than "castelamarin."

In common with most higher plants, *Castela Nicholsoni* contains tannic acid. It also contains a small amount of oil and considerable mucilaginous matter, which occurs in the hypodermal tissue cells, especially abundant in the hypoderm of the leaves. The mucilaginous matter is colorless and tasteless and is readily soluble in water; forms an emulsion with chloroform but is thrown down by 50 per cent. alcohol. Among the other inert constituents present are a small amount of resin and considerable chlorophyll. As stated, the mucilaginous matter is especially abundant in the leaves and since this substance is undesirable in preparations intended for hypodermic administrations, and since the leaves are small and readily drop off, it is suggested that the leaves be discarded altogether, in making the purified dry extract.

The older branches are literally covered with crustose lichens and also foliose and fruticose forms, and since these saprophytes may contain toxic or otherwise therapeutically objectionable substances, it would appear highly desirable to remove the outer bark layers of the older branches by some suitable process, using only the inner parenchymatous and woody tissue; at least this would be desirable in preparing the drug for making the preparations intended for hypodermic use. The terminal branches of the younger plants or the recent growth (one to two years) are comparatively free from lichens.

In common with desert plants generally, *Castela Nicholsoni* is quite rich in

mineral salts, as chlorides, sulphates and carbonates, and the removal, wholly or in part, of these constituents, should be taken into consideration by pharmaceutical manufacturers.

Pharmacology and Toxicology.—Bosman speaks of castelin as the active principle (therapeutically) of *Castela Nicholsoni*, but so far no tests have been made to demonstrate that castelamarin is *not* the active principle despite the statement by Bosman that this substance is pharmacologically quite inactive (excepting the action on the coronary circulation). No observations are recorded as to the pharmacologic action of castelagenin nor is it known to what extent this product of the hydrolization of castelin occurs or develops naturally in the dry and aging drug. The indications are that all three substances occur in the growing plant, but that after drying and especially on exposure to light and moisture, and also during pharmaceutical manipulation, the castelin is gradually converted into castelagenin. Further investigations are necessary to clear up these points.

All of the pharmaceutical preparations, as well as the infusion, contain the three substances named (castelin, castelagenin, and castelamarin), as well as certain salts and also inert constituents. According to numerous laboratory tests the purified (detannated and degummed) solid extract which consists largely of the three constituents named is only $^1/_{20}$th or $^1/_{25}$th as toxic as is emetin hydrochloride. Death is due to gradual general paralysis, respiration ceasing before the action of the heart. The heart (in frogs) stops in diastole (auricular as well as ventricular). The comparative study of the toxicity of the solid extract of Castela and of emetin hydrochloride gave the following results.

Paramecial method (3 minutes)	1–25
Frog method (1-hour periods)	1–20
Gold fish method (1-hour periods)	1–22

It is rather remarkable that Castela and emetin should produce closely similar reactions in *Ameba caudatum*. Motion is slowed, trichocysts are ejected early and string out behind the organism as it moves along. Next there is a zig-zag forward motion, then a pin-wheel motion, finally all motion (excepting ciliary) ceases, the plasmic contents are completely expelled and only the external membrane, with the cilia still in active motion, remains.

Bosman made a series of tests, with the purified castelamarin, on isolated tissues and on tissues *in situ*, with apparently negative results. Strengths of solutions up to 1:500 were used but without any appreciable effects on the isolated intestine and the uterus of the non-pregnant cat. A negligible increase in tone was indicated. The most striking effect following the perfusion on the isolated mammalian heart with a 1–2000 solution was the constriction of the coronary vessels. This was indicated by a great retardation in the outflow, which was actually reduced to one-third and less. The conclusion reached by Bosman is that the bitter principle of Castela was a substance of low toxicity and of only slight pharmacologic activity.

Dr. P. I. Nixon of San Antonio, Texas, made some tests with the fluid extract of Castela on the amebæ of dysentery, declaring that this organism was very sensitive to the action of the drug, killing promptly in very high dilutions. The following is quoted from his article: "I give the results of a few experimental observations to show the amebicidal action of Chaparro amargosa. Under the microscope, 1:10,000 dilution of the detannated fluid extract at body temperature caused all *Entamoebae*

histolytica to cease moving instantly and to assume a spherical shape with sharp differentiation of ectoplasm and endoplasm; 1:100,000 dilution required from thirty to sixty seconds to accomplish the same results, and 1:1,000,000 from one to three minutes." These observations could not be verified by others, including the writer. In fact the usual saprophytic forms of amebae are even more resistant to the action of Castela than are the paramecia. In a dilution of 1:12 of the solid detannated and degummed extract of Castela the amebae were not killed for some time (ten minutes or longer) although there was noticeable an increase of the ectoplasmic zone while the endoplasm appeared to remain unchanged. A dilution of 1:9 killed *Paramecium caudatum* in three minutes; while the same organism was killed within the same period of time by a dilution of 1:225 of emetin hydrochloride, thus proving the latter substance to be 25 times as toxic as the former. However, it has been demonstrated repeatedly that the toxicity of a drug is not necessarily proportional to its therapeutic activity; nor does it follow that a therapeutic agent must yield test-tube or laboratory results in order to be of use therapeutically. Whether or not Castela kills the amebae of dysentery in a test-tube or on a slide is after all of minor importance. The clinical results have shown that in *Castela Nicholsoni* we have a drug of great promise in the treatment of amebic dysentery. It has apparently given results in cases that did not respond to emetin. It is far less toxic than is emetin. The prolonged use of ipecac in resistant cases of amebic dysentery has resulted in marked toxic manifestation, from which the patients fortunately recover completely as soon as that drug is discontinued. No such toxic effects follow the use of Castela. Dr. Boyers (Berkeley, California), in a verbal report, declared that the infusion of Castela gave rise to intestinal disturbances, without, however, giving particulars. Large doses (3 drachms of the fluid-extract) taken by the writer produced no marked disturbances of any kind. There was a slight laxative effect and the appetite was somewhat increased. The slight toxic effects reported by Dr. Boyers may have been due to the use of old lichen-covered stems. The rather negative results in amebic dysentery reported by Dr. Boyers may also have been due to the use of old more or less inert material.

Therapy of Castela Nicholsoni.—As has already been indicated, the principal use of the drug is in the treatment of amebic dysentery. Whether or not it is also of use in the bacillary forms of dysentery has not been definitely ascertained although Dr. Nixon declared that it is useless in such cases. The Nixons used the drug in the form of the infusion (of the color of weak tea) per mouth (teacupful doses) and also as enemas, continuing the treatment for some time after the stools have returned to normal. The beneficial results are apparent almost immediately. On the first sign of recurrence, the treatment is to be repeated. For details of the method of using Castela in amebic dysentery those interested should consult the articles by Knox, Nixon, and Sellards and McIver.

The therapeutic value of the drug in malaria has not been ascertained. It would be well worth while to give it a trial in this disease. It is suggested that for such a trial the dry extract be administered hypodermically in doses of not less than one gram (15 grains) daily, about the time the chill is to come on (sporulating stage of the malarial protozoan), and continued for a week at least.

Dr. Van Hoosen of Chicago tried the dry purified extract in a case of carcinoma of the uterus which did not respond to the action of emetin hydrochloride. The

drug (30 grains) was dissolved in 50 cc. normal saline and injected under the breast (connective tissue). Within an hour after the injection of the first dose there was some vomiting without intestinal disturbance, but no other untoward reactions. Vomiting did not recur on subsequent injections of like amounts, and it is believed that the vomiting following the initial dose was psychically reflex (anticipatory), as the patient had previously vomited after each dose of emetin hydrochloride. The outcome of the treatment in this case was not announced to the writer despite several inquiries verbally and *in lit.*

Pharmaceutical Preparations.—Sharp and Dohme of Baltimore, for a number of years, have been marketing the extract, the fluidextract, and gelatine coated pills of *Castela Nicholsoni*. The extracts are very dark in color and intensely bitter and somewhat astringent, but there is no acridity or pungency and even the most delicate tissues are not disturbed by it. The dose of the extract is 2 to 3 grains, of the fluidextract one drachm, and 1 to 3 pills. The fluidextract as well as the solid extract, despite the extreme bitterness, recall the taste of glycyrrhizin or licorice somewhat. The infusion (in hot water) as used by Dr. Nixon has the color of tea and is, of course, also intensely bitter. The author prepared a purified solid extract intended for hypodermic administration, as follows.

Extract for six hours one kilo of the coarsely broken recently gathered dry drug, in two kilos of hot distilled water, with occasional stirring. Filter through cotton and to the filtrate, when sufficiently cool, add 10 grams of powdered egg albumen, stirring until the albumen is mostly dissolved. Bring to a boil. The coagulating albumen takes up the tannic acid and the coarser impurities. Filter through one layer of coarse filter paper. Evaporate the filtrate to one-half volume, or less, at reduced pressure; and add an equal volume of 97 per cent. alcohol which throws down (coagulates) the mucilaginous matter, which is then removed by filtration, again using coarse filter paper, and then evaporate the detannated and degummed aqueous extract to dryness at reduced pressure, using porcelain-lined evaporating dishes. The dry extract is of dark brown color, very brittle and highly hygroscopic. The powder is of a rather light cinnamon brown color and must be kept in dry air-tight containers. On exposure to the air the powder soon becomes sticky due to the absorption of atmospheric moisture. It is readily soluble in water (either distilled or hydrant water, or in normal saline). For hypodermic use, dissolve the required amount of the powder in from 15 to 50 cc. of distilled water or in normal saline, and inject slowly. There are neither local nor systemic reactions. In a female cancer patient, a dose of 2 grams (30 grains), given interstitially (under the breast), vomiting (without purging) followed within an hour after the first dose, but subsequent injections (also 30 grains), were without any disturbing reactions of any kind (from verbal and *in lit.*, reports of Dr. van Hoosen of Chicago). The writer administered to himself 10-grain doses hypodermically on several occasions, without any appreciable reactions, either local or general. As far as known to the writer, no one else has administerd preparations of Castela hypodermically.

The Nixons originally used the freshly prepared tea of Castela in the treatment of dysentery. The infusion as well as the decoction deteriorate very readily on standing, due to bacterial invasion. The solid extract keeps fairly well, but it is nevertheless advisable to add a small amount of trikresol (0.25 per cent.) to the dry extract intended for hypodermic use.

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Plate I. Gross morphology of *Castela Nicholsoni*, Hooker. (*E. S. del.*, after Hooker.) A, portion of female plant; B, portion of a male plant; a, unexpanded flower; b, female flower, with 3 abortive stamens; c, single abortive stamen; d, stamens; e, single stamen; f, fruit (drupe); g, drupe cut open to show the seed with endocarp; h, drupe showing seed in position; i, transversely cut drupe; j, embryo; k, leaf, somewhat enlarged.

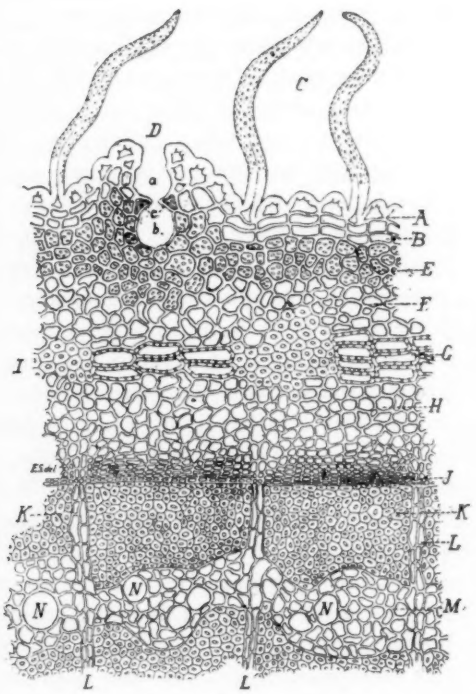

Plate II. Transverse section of the stem of *Castela Nicholsoni*, Hooker, ×450 (*E. S. del.*). A, epidermal layer; B, hypodermal layers; C, trichomes; D, water pores; a, antechamber, b, reservoir; c, guard cells; E, chlorophyll bearing parenchyma; F, outer bark parenchyma; G, sclerenchyma cells; H, inner bark parenchyma; I, groups of bast cells; J, cambium; K, wood parenchyma; L, medullary-rays; M, water-storing tissue; N, ducts, porous.

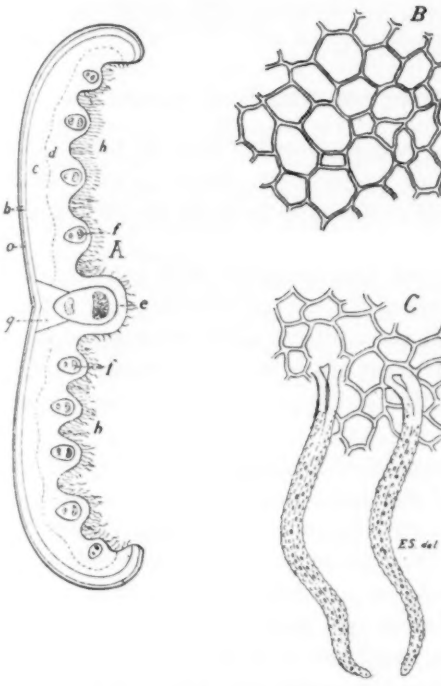

Plate III. Histology of leaf. B and C, ×450; A, ×60. (*E. S. del.*) Transverse section of leaf, diagramatic; a, epidermis; b, hypoderm; c, palisade tissue; d, spongy tissue, midrib; f, vascular bundles; g, mechanical tissue. B, upper epidermal cells, vertical view; C, lower epidermis, with trichomes, vertical view.

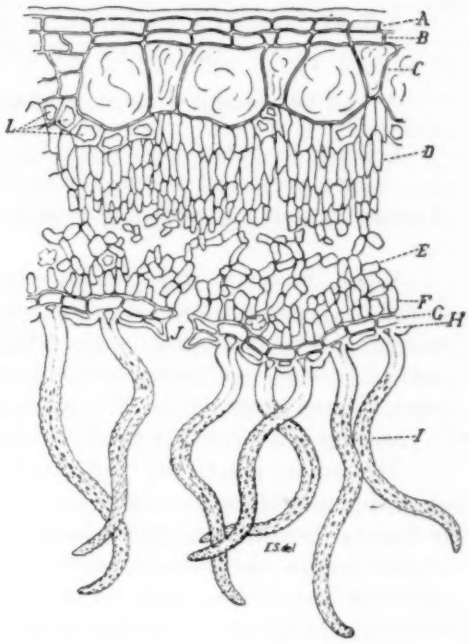

Plate IV. Transverse section through leaf, ×450. (*E. S. del.*) A, epidermis; B, first hypodermal layer; C, second, mucilage bearing hypodermal layer; D, palisade tissue; E, spongy tissue layer; F, single row of lower palisade tissue; G, lower hypodermal layer; H, lower epidermal layer with trichomes (I) and stomata (J); L, prismatic crystals of calcium oxalate.

Asa Gray, "Genera of the Plants of the United States," II, 153 (plate 158) (1849).

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A NOTE ON THE CHEMICAL COMPOSITION AND BIOLOGICAL ACTIVITY OF LIQUOR FOLLICULI.

BY FREDERICK W. HEYL, MERRILL C. HART AND WILBUR B. PAYNE.

Fellner has published several[1] interesting articles showing that the subcutaneous or intraperitoneal injection of the lipoids of the placenta, corpus luteum and of testes[2] into immature female rabbits stimulates the growth of the uterus in each case.

When, however, these lipoids were injected into immature male rabbits, the size of the growing testicle was restrained.[3] He also observed that the time of the beginning of spermatogenesis was delayed. If these injections were continued, the testicular connective tissue widened to the detriment of the lumen, in which detritis masses were conspicuous. The general condition of the testes is said to be similar to that noted as a result of the Roentgen ray.

Herrmann[4] practically duplicated the histological findings of Fellner so far as observing the stimulation of the growth of the female genitals upon injection of lipoidal preparations from placenta and corpus luteum. Herrmann, however, elaborated the methods of purification of the injected lipoid. He prepared a phosphatide-free fat, from which he isolated the unsaponifiable fraction. This proved to be active. The same procedure on the two lipoids led to similar results indicating the possible identity of the active constituents of placenta and corpus luteum. Herrmann states (page 26) that when the lipoids of ovarian residue were examined in parallel with the above-mentioned extracts dissolved in olive oil that they proved to be physiologically active[5]. Herrmann gives the boiling point of his substance as 193° to 230° at 0.06 mm., and states that it gives cholesterol color tests. Most of Herrmann's physiological tests were made in immature and castrated animals. In general he gave five injections (10 days time) amounting to 0.24 g. and observed the maturity of the genitals in 8-week old rabbits.

Fränkel[6] and Fonda have followed up Herrmann's work but the fractionation does not yield a fraction of constant boiling point, all further work being done on a fraction that boiled at 194° at 0.06 mm., but closely associated with substances of far different composition. To the intermediate fraction boiling at 194° the formula $C_{32}H_{52}O_2$ is assigned. The activity appears to be lost on distillation.

Goetsch[7] reported that the feeding of anterior pituitary lobe produced sexual maturity in young rats even more rapidly than corpus luteum. It is to be noted that Goetsch reports growth stimulation with corpus luteum, however.

Frank[8] reported results with placenta and corpus luteum lipoids in agreement with Herrmann, stating that the latter is richer in active lipoidal material.

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[1] *Centrabl. f. Allgemeine Path. u. Path. Anat.*, Aug., 1912. *Arch. Gyn.*, 100, 641 (1914), and *Arch. ges. Physiol.* (*Pflügers*), 189, 199 (1921).

[2] Thymus lipoids also gave positive results, in contrast to brain lipoids.

[3] Herrmann and Stein, *Wien. klin. Wochenschr.*, 6, 25 (1916).

[4] *Monatsch f. Geburts. u. Gyn.*, XLI, 1 (1915).

[5] Fellner reports the reverse.

[6] *Biochem. Zeit.*, 41, 379 (1923).

[7] *Surg. Gyn. and Obstet.*, 25, 229 (1917).

[8] *Surgery, Gyn. and Obstet.*, 329, (1917).

Frank states that the chemical substance which produces these changes is thermostable, very resistant to alkalies and acids.

Recently Allen and Doisy[1] *et al.*, using chemical methods which lead to the unsaponifiable fraction of the lipoids found in the follicular fluid of sows, have demonstrated the presence of active material in this fluid. And when using corpus luteum they have been unable to demonstrate, by the method of Stockard and Papanicolau,[2] the production of estrus in spayed rats. Frank[3] states that corpus luteum gives positive anabolic results, identical with those obtained by the use of follicular fluid.

The evidence in these papers points out the importance of a fat fraction which has received very little attention. The growth-stimulating substance which has apparently a specific selective action on certain tissue, such as the uterus, is always found in the syrupy filtrates which systematically result after all the cholesterol (or phytosterol in plant fats) has been removed from the unsaponifiable. These syrups have up to this time failed to yield any substances of interest (except cetyl alcohol etc.) and are usually discarded.

It is of interest to point out in this connection that evidence[4] is accumulating that the antirachitic substance in cod liver oil is similarly a sterol or cholesterol derivative found in this fraction. It is in this fraction that we find substances having the property of emitting ultraviolet rays upon spontaneous oxidation. The general growth promoting vitamine A, and the more specific growth stimulating oil-soluble substances of the glands, which we designate as hormones are probably stored in these particular oil solutions by the animal body and have very similar properties. That these hormones can be varied by dietary revisions has been pointed out by Evans and Bishop.[5]

The œstrus cycle is in fact very sensitive to dietary deficiencies and it would appear to be a well-founded hypothesis that the content of these active substances in commercial products depends on the diet of the animals from which they were prepared; that they are in fact, like the carotins, not elaborated by the animal.

We have been studying this fraction of corpus luteum and some other glands and after the publication of the Allen and Doisy paper we were interested in finding out what the prospects might be of utilizing the follicular fluid of the sow as a source of supply of this material, but the yield is extremely low; only 1.2% total fat was found as compared with 0.7% of the unsaponifiable fraction, cholesterol free in corpus luteum.

Incidentally as we could find no report in the literature we have conducted a brief analysis of the liquor folliculi, a résumé of which is found at the end of the article.

EXPERIMENTAL.

Corpus Luteum.—Previous work, in which 5,673 g. of desiccated glandular material was exhaustively extracted with cold acetone gave, after the separation

[1] *J Biol. Chem.*, 61, 711 (1924). *Am. J. Anatomy*, 34, 133 (1924); *ibid.*, 34, 445 (1924).

[2] *Am. J. Anat.*, 22, 225 (1917).

[3] *J. A. M. A.*, 81, 1133 (1923).

[4] T. F. Zucker, Pappenheimer, Barnett, *Proc. Soc. Exptl. Biol. Med.*, 19, 167 (1921); Steenbock, Jones and Hart, *J. Biol. Chem.*, 55, XXVI (1922); also 46, XXXII (1921).

[5] *J. A. M. A.*, 81, 889 (1923).

of phosphatides, a fat fraction yielding 720 grams. This fraction, after removal of free fatty acids by shaking the ethereal solution with alkali, was saponified and there resulted 110 grams of unsaponifiable material containing 72 grams cholesterol (both as ester and free). The faction under discussion therefore amounts to about 38 grams or 0.7% of the desiccated gland.

In comparing this yield with follicular fluid we found that 7.3% solids of this fluid yielded 0.088% of fat so that this substance in dry form will yield 1.2% of fat, *i. e.*, both saponifiable, free fatty acids and cholestrol. This quantity of fat upon further analysis will be found to contain much less than 0.7%, found in the corpus luteum fraction referred to above.

	Fat.	Unsaponifiable.	Unsaponifiable, minus cholesterol, etc.
100 Gm. Corpus Luteum	= 12.33%	= 1.93	0.7
100 Gm. dry Follicular Fluid	= 1.20%	...	...

Follicular Fluid.—The material examined consisted of the liquor folliculi from hog ovaries, obtained through the kindness of Dr. D. Klein of the Wilson Laboratories. A sample of follicular liquid, consisting of 230 cc. was immediately placed with 460 cc. of ethyl alcohol. A heavy white precipitate of protein formed. This was centrifuged off and washed thrice with 500 cc. of 75 per cent. alcohol, twice with 500 cc. of absolute alcohol at 40° C., and twice with 500 cc. of dry ether. It was then dried to constant weight *in vacuo*. It was a white impalpable powder weighing 14.9870 grams = 13.93 grams dried at 110° or 6.06%.

A sample was dried to constant weight at 110° C.
Sample, 0.5188 gram, loss at 110° C., 0.0367 gram moisture, 7.07%.

The dry protein[1] was analyzed for nitrogen by the micro-Kjeldahl method and for phosphorus by the Neumann method.

Samples 0.0349, 0.0337; *N*/50 ammonia, 17.90; 17.43 cc.
Found N, 14.37; 14.49
Samples 0.1660, 0.1776; *N*/20 sodium hydroxide, 2.80; 3.18 cc.
Found P, 0.09; 0.10.

The alcoholic ethereal filtrates from the protein were evaporated under reduced pressure to a volume of about 500 cc. A flocculent precipitate separated on standing in the ice box. This was centrifuged off, washed with alcohol and ether and dried *in vacuo*. This was a brownish solid weighing 0.6554 Gm. = 0.28% further or 6.34% total protein. This material appeared to be impure protein and was not further analyzed.

The filtrates and washings from the above precipitate were concentrated again under reduced pressure and made up to a volume of 500 cc.

10 cc. gave 0.0446 gram solids. Total solids (not protein) 2.2300 grams = 0.97%
0.0446 gram solids gave ash 0.0290 gram. Total ash, 1.450 grams = 0.63%
Organic material 0.7800 gram = 0.34%
Samples 5.00 cc., 5.00 cc. *N*/50 ammonia 1.51 cc.; 1.67 cc.
Total non-protein N, 0.0445 gram = 0.019%.

[1] The nitrogen distribution will be reported later.

The remainder of the 500 cc. (480 cc.) was taken down to 10 cc.; 75 cc. of absolute alcohol and 75 cc. of ether were added. A gummy precipitate formed which was centrifuged off. This solid was very thoroughly washed with alcohol and ether. The filtrates and washings were then taken down to about 3 cc. at 40° C., treated with 5 cc. of absolute alcohol and 50 cc. of dry ether. More of the gummy precipitate formed. This was washed with alcohol and ether, joined with the first precipitate, dissolved in water in which it was practically all soluble, filtered and evaporated to dryness. The material consisted of cubical crystals, presumably sodium chloride and varnish-like extractive material.

Proximate analysis of extractive fraction.—It was dissolved in water and made up to a volume of 100 cc. (1 cc. = 2.208 cc. follicular fluid).

Total nitrogen.—Five cc. by micro Kjeldahl required 5.94 cc. $N/50$ acid, equivalent to 0.001663 gram N. This amounts to 0.015% of the original follicular fluid.

Ammonia and urea.—One cc. (=2.208 cc. follicular fluid) was examined by the urease method of Marshall[1] and required 0.84 cc. of $N/50$ acid, equivalent to 0.000235 Gm. urea N equivalent to 0.0106% urea N in follicular fluid. The *urea* content is 0.023% since urea contains 46.6% nitrogen.

The ammonia blank made on 2 cc. (=4.416 cc. of follicular fluid) required only 0.1 cc. N 150 acid and was not calculated.

Creatinine (total).—One cc. (= 2.208 cc. of follicular fluid) + 1.8 cc. 25 % H_2SO_4 + 6 cc. water was heated on the steam-bath and made up to 10 cc.[2] Of this 9 cc. (= 1.99 cc. follicular fluid) was neutralized and read against a standard creatinine solution containing 0.1 mg. Colorimetrical readings showed 0.000105 Gm. creatinine, or 0.005% of the follicular fluid = 0.0019% creatinine nitrogen (× 37.2%).

Phosphotungstic acid precipitable bases.—The urea N (0.0106%) + creatinine (0.0019%) = 0.0125% N of a total of 0.015%.

The remainder of the solution, 85 cc. (= 187.7 cc. follicular fluid) was made acid with 5% sulphuric and precipitated with phosphotungstic acid. The small precipitate was removed by centrifugation, decomposed with baryta in the usual manner, and the filtrate concentrated and then made up to 50 cc.

Ten cc. (37.5 cc. follicular fluid) required by micro-Kjeldahl 2.6 cc. $N/50$ acid equivalent to 0.000728 Gm. N = 0.0019% follicular fluid.

The phosphotungstic precipitate yielded but little creatinine, therefore most of this is derived from the original presence of creatine.

Two cc. (= 7.5 cc. of follicular fluid) + 1.8 cc. 25% H_2SO_4 + 5 cc. water was hydrolysed on the steam-bath and made up to exactly 10 cc. Of this 9 cc. (= 6.75 cc. of original follicular fluid) when compared to a standard of 0.05 mg. creatinine showed the presence of 0.028 mg. equivalent to 0.000414% creatinine, or 0.00015% creatinine N. Obviously the creatinine in the precipitate is so slight that it indicates the original presence of creatine.

We may therefore conclude that the basic constituents precipitable with phosphotungstic acid (not creatine) amount to approximately 0.0019% N.

The filtrates and washings from the above alcohol plus ether insoluble material were taken down to a syrup and taken up again in 5 cc. of ether, in which it was completely soluble, and the phosphatides precipitated with 20 cc. of pure acetone. A white flocculent precipitate of the acetone insoluble lipoids was obtained. The mixture was cooled and the phosphatides centrifuged off. This precipitate was taken up in 2 cc. of ether and reprecipitated with 8 cc. of acetone. The mixture was

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[1] *J. A. M. A.*, 62, 1558 (1914).

[2] Janney and Blatherwick, *J. Biol. Chem.*, 21, 579 (1915); Falk, Baumann, and McGuire, *ibid.*, 37, 528 (1919).

again cooled and the precipitate centrifuged off. It was washed with 5 cc. of acetone and dried *in vacuo*. This weighed 0.0613 Gm. (= 0.027% phosphatide). It was analyzed for phosphorus and nitrogen.

Sample, 0.0219 Gm.; 4.14 cc. $N/20$ sodium hydroxide: P, 1.05% of Phosphatides.
Sample, 0.0371 Gm.; 1.59 cc. $N/50$ ammonia: N, 1.20% of Phosphatides.
Nitrogen: phosphorus = 2.53:1.

There was not sufficient material for emulsification with water so the high nitrogen of this fraction was probably due to contamination of a carnithin[1] like nature.

The filtrates and washings from the above phosphatide, containing the fats, cholesterol, etc., were concentrated down to a syrup, taken up in 2 cc. of dry ether and treated with 10 cc. of pure acetone. The solution turned slightly cloudy on cooling. It was filtered and made up to a volume of 20 cc. It contained 0.195 Gm. equivalent to 0.088% of the follicular fluids.[2]

Sample, 2 cc.; Solids 0.0195. Total solids, 0.1950 Gm.
Sample, 2 cc.; 0.91 cc. $N/20$ sodium hydroxide, P, 0.000050 Gm.
P = 0.26% of fat fraction.
Sample, 2 cc.; 3.03 cc. $N/50$ ammonia. N, 0.00085. N = 4.35% of fat fraction.

Material thus prepared was used for physiological testing.

We have been testing the effects of glandular feeding and of various corpus luteum fractions on the œstrus cycle in guinea-pigs, using the methods of Stockard and Papanicolau. According to Allen,[3] subcutaneous injections of oil solutions of the fat fraction of follicular fluid into spayed mice and rats, in which the anabolic phase of the œstrus cycle is 2 to 3 days, produced œstrus in 3 injections (containing roughly 1 to 2 milligrams of the fat fraction). Continued injections caused an extended period of œstrous growth (freedom from leucocytic infiltration). This test is therefore based on the stimulation of growth in the vaginal and uterine mucosa by the injection and the subsequent induction of metoestrum by its withdrawal.

The guinea-pigs used in these experiments showed an average dioestrous cycle of 15.3 days (22 periods). The injections of the fat fraction of follicular fluid were made subcutaneously, using an oil base. Three injections were made in each experiment. When total quantities not in excess of 0.05 Gm. (fat fraction) were injected, no change in the cycle was observed. In larger quantities, however, (0.06 gram) the œstrous cycle was prolonged. With this quantity the period was extended to 18 days, while the average of those receiving the smaller doses average 15.3 days, no lengthening whatever being observed. All these injections were made at three-day intervals, beginning at the 8th day from the last heat period.

The proximate analysis of follicular fluid may be stated as follows:

	Per cent.
Total Solids	7.310
Protein	6.340

[1] H. MacLean, *Biochem. J.*, 9, 353 (1915).

[2] Doisy *et al.*, report, *J. Biol. Chem.*, 61, 721 (1924), their active fraction in purified extracts to vary from 0.02 to 0.19%.

[3] Allen *et al.*, *Am. J. Anat.*, 34, 149 (1924).

Solids not protein	0.970
Ash	0.630
Lipoids (total)	0.115
Phosphatides (crude)	0.27
Fat, cholesterol, etc	0.88
Total extractive N	0.019
Lipoid N	0.004
Extractive N	0.015
Urea N	0.0106
Creatinine	0.0019
Basic N	0.0019

It is therefore shown that of the total solids in follicular fluid, the chief mass is protein. The concentration of the salts are apparently somewhat lower than in the blood and a considerable quantity of urea is present, but a trace only of phosphotungstic precipitable substances. The fat fraction amounted to 0.088%.

LABORATORIES OF THE UPJOHN COMPANY,
KALAMAZOO, MICH.
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A PALATABLE COD LIVER OIL CONCENTRATE POSSESSING THE THERAPEUTIC PROPERTIES OF COD LIVER OIL.*

BY HARRY E. DUBIN.

The therapeutic value of cod liver oil has been common knowledge for a great many years, but until recently its use was on a purely empiric basis.[1] With the indisputable proof at hand that cod liver oil is really a specific in the treatment of rickets, interest has been aroused in the possibility of isolating the active principle responsible for its therapeutic effect.

Regarding the mechanism of the action of cod liver oil, investigation has revealed the fact that the metabolism of calcium and phosphorus is in some way favorably influenced. It has also been found that cod liver oil has a stimulating effect on the intestinal mucous membrane and possibly on the formation of blood platelets.

Whatever the mode of action, the efficacy of cod liver oil is unquestioned. While it is a specific remedy for rickets, it has in addition a general restorative and vitalizing value. The vitamines inherent in cod liver oil are necessary for growth and health and for the normal development of bones and teeth. They promote growth and development in the adolescent period and are of great help in combating infections, by increasing body resistance.

The healthy adult does not need cod liver oil, but there are numerous cases where it could be used to advantage. While the adult does not suffer from active

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* Detailed experimental data obtained by Dr. Dubin and Dr. Funk appears in *J. Metabolic Research*, 4, 467 (1923).

[1] The results of the clinical investigation made by Dr. Louis Fischer, Director of the Infantorium and Nursery of the Heckscher Foundation, New York City, are published in *J. Metabolic Research*, 4, 480 (1923).

rickets, the same dietary deficiencies leading to its development in the child may also exist in the adult and impair his health.

The medicinal properities of cod liver oil were at first thought to be due to its nutritive value as a fat. Later its value was attributed to its mineral content. Recent research, however, makes it impossible to doubt that the therapeutic action of cod liver oil is due solely to the antirachitic and antiophthalmic vitamines present.

Recognizing the therapeutic efficacy of cod liver oil, attempts have generally been made to overcome its objectionable features, such as nauseous taste and odor. The customary procedure has been to prepare extracts and emulsions of various kinds. However, the usual alcoholic extract has little or no therapeutic value, while the emulsion is active only in proportion to its oil content; as for palatability—there is very little decided improvement.

Attention has therefore been directed towards the isolation of the active principle. Many investigators have been occupied with this problem and appreciable progress has been reported. We have been engaged in this work for almost three years, and although we have not actually identified the active principle of the oil, *we have nevertheless succeeded in preparing a highly concentrated product, free from oil, practically odorless and tasteless, non-toxic and equal in therapeutic value to fresh cod liver oil.*

Briefly, the method involves extraction of cod liver oil with an organic acid such as acetic or formic acid. The acid extract is freed from acid and the oil remaining, amounting to about 5 per cent. of the original cod liver oil, is saponified with alcoholic soda or potash. The soaps are extracted with ether and the ether evaporated off, leaving the active cod liver oil concentrate. The destructive effect of oxidation is avoided by carrying out the process in the absence of air. Exclusion of air is essential to assure the stability of the preparation.

By this method, from 1000 Gm. cod liver oil it is possible to obtain 0.1 Gm. concentrate which is practically as potent as the original quantity of fresh cod liver oil.

In the crude state, the cod liver oil concentrate is a brown semi-crystalline pasty mass. In combination with sugar it appears as a creamy white powder which may be compressed into tablets of any desired size and dosage. Because of the high degree of concentration, it is feasible for example, to prepare a 1-grain tablet to be the equivalent of 1 tablespoonful of fresh cod liver oil.

Almost 700 animal experiments have been carried out to prove the value of this cod liver oil concentrate. When rats are placed on a rickets-producing diet, they develop rickets in about 30 days. On administering an amount of cod liver oil concentrate corresponding to as little as 0.028 Gm. cod liver oil, the rachitic manifestations disappear in about 3 weeks. The same amount of concentrate will also prevent rickets in animals maintained on the above diet. In other words, the concentrate can act both as a curative and as a prophylactic agent.

The accompanying chart and radiographs illustrate briefly the antirachitic action of the cod liver oil concentrate, using the prophylactic type of experiment.

Each of the animals represents a series placed on the indicated rickets-producing diet. Rat No. 693, the control, developed rickets, while the others, receiving either cod liver oil or the cod liver oil concentrate, remained normal.

Rat.	Weight—Gm. June 6, 1924.	July 8, 1924.	Gain.	X-Ray.	Substance administered daily.	Diet Pappenheimer-Zucker diet D.	Gm.
680	42	75	33	Normal	28.0 mg. cod liver oil	Patent flour	80.9
684	40	64	24	Normal	0.074 mg. concentrate equal to 28.0 mg. cod liver oil	Egg albumin	10.0
						Butter fat	5.0
693	40	92	52	Rickets	Control	Salts	4.1

In the rachitic rat No. 693, note the enlarged epiphyses, A, and lack of calcification, as compared with the well-calcified bones, B, of the other rats.

Rat No. 680. Rat No. 684. Rat No. 693.

The antiophthalmic effect of the cod liver oil concentrate is illustrated by the following typical experiment:

Rat No. 726 was placed on a diet adequate in every respect except as to fat-soluble vitamines. At the end of 2 months the animal showed marked ophthalmia and had stopped growing. Daily administration of an amount of cod liver oil concentrate corresponding to 0.028 Gm. cod liver oil was started. The animal promptly resumed growth and at the end of 14 days its eyes appeared normal.[1]

Clinical experiments have also been made, showing clearly by means of X-ray and otherwise that the concentrate is as effective in children as in animals.[2]

By means of such a concentrate it is a simple matter to institute cod liver oil therapy in a more agreeable form, especially in the numerous instances where fresh cod liver oil is not tolerated.

There seems to be no good reason why infants, as early as one month old, should not be given cod liver oil or cod liver oil concentrate as a prophylactic against rickets.

It would be possible, therefore, to decrease the incidence of rickets to negligible proportions, and remove it as a menacing factor in the development of the child. At the same time, other nutritive disturbances due to lack of the vitamines found so abundantly in cod liver oil would be eliminated.

In this connection it is interesting to note that respiratory infections are quite prevalent among babies whose diets are deficient in these vitamines. The routine administration of cod liver oil to such babies has been strikingly effective in producing an immunity against these infections.

It has thus become increasingly evident that cod liver oil therapy, emerging

[1] Detailed experimental data obtained by Dr. Dubin and Dr. Funk appears in *J. Metabolic Research*, 4, 467 (1923).

[2] The results of the clinical investigations, made by Dr. Louis Fischer, Director of the Infantorium and Nursery of the Heckscher Foundation, New York City, are published in *J. Metabolic Research*, 4, 480 (1923).

from the haphazard to the scientific stage, is taking its place as an important element in the management of infant nutrition.

DISCUSSION.

Arno Viehoever: I had the privilege of looking over three papers submitted to me by Dr. Dubin for perusal. My first suggestion would be that the author reconsider the presentation of the paper to be submitted to the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION because in that paper there is only a brief abstract without any experimental data being given. I feel that all the members of the Association are interested in that work, and many of you no doubt will want to be informed as we have been this morning, as to the evidence which has been obtained in an experimental way on animals. I feel that the work which has progressed for three years has certainly produced results. There are, as the author mentioned, other extracts on the market.

He also points out in his paper that four methods exist. One is the saponification of the original oil, necessitating working in very large quantities. He also pointed out that another method consists in saponification of the alcoholic extract. The third method which he did not bring out this morning was developed by himself and Dr. Funk, and that is hydrogenation of the oil and then subsequent extraction. And finally, there is the acid extract of cod liver oil, the subject of the present paper.

It was stated that either acetic or formic acid had been found to be useful.

I may also say that after saponification of this acid extract, the residue is extracted with ether and in that way a concentrate containing the valuable vitamines are obtained. I may further say that this cod liver oil concentrate has been found to be free of nitrogen sulphur and phosphorus. Only the presence of carbon, hydrogen and oxygen has been demonstrated.

One of the questions I would like to ask at the end of my remarks is whether there is any close chemical relationship between the cod liver oil concentrate and the substance isolated from yeast by Dr. Eddy, who pointed out that the yeast vitamine contains nitrogen.

I was interested to find out that a distinct difference exists between the saponification of the original oil and saponification of the alcoholic extract.

I certainly want to compliment the author on the progress of the work which is evident from a study of his three papers and from the demonstration this morning.

A. C. Taylor: I would like to ask the author if I correctly understood that he distinguishes in his experiments between the antiophthalmic vitamine and the antirachitic vitamine which are recognized to-day as being distinct? Does the alcohol fail to remove both of them, or only the one; and does the acid extract that he speaks of remove both or only one; and does the concentrate contain both of these or one?

Dr. H. C. Wood: I certainly was very much interested in this paper. It represents a very marked advance and is a very important record.

I want, however, to protest against one phrase that the reader of the paper used, and that is when he speaks of this concentrate as representing all the therapeutic value of cod liver oil. It would perhaps be more accurate to speak of it as antirachitic value of cod liver oil. A very large proportion of the value of cod liver oil rests in the peculiar character of the fat which composes it. The fat of cod liver oil is more nutritious than most of our fats, because it is more readily absorbed from the intestinal tract than other fats. I maintain no preparation of cod liver oil which does not contain the fats can represent all the therapeutic value of the oil.

L. E. Warren: I would like to ask the author for a little more detail in regard to the method of the manufacture of this preparation. It seems to me that in the details that he has given and in the little more enlarged details that Dr. Viehoever has given, no chemist among you could follow his method and reproduce that preparation.

Robert J. Ruth: I would like to have a word concerning the stability of the preparation.

Harry E. Dubin: As regards Dr. Viehoever's remarks on the relationship between the cod liver oil vitamines and yeast vitamine, it is recognized that yeast contains one of the so-called water-soluble vitamines, while the cod liver oil vitamines are fat-soluble. Cod liver oil will cure rickets and ophthalmia, whereas yeast will cure beriberi. The available evidence is against any close chemical similarity between these two types of vitamines.

The only possible connection is that all vitamines are necessary for complete growth. The antiophthalmic vitamine has always been called the growth-promoting vitamine. We

must remember, however, that real growth on any particular diet will not take place unless all the vitamines are present. It is evident, therefore, that any one of the vitamines, or for that matter the mineral content of the diet, may be the limiting factor of growth.

Regarding the questions raised by Dr. Taylor, the alcoholic extract of cod liver oil, while it is antirachitic, is not antiophthalmic. The oil remaining after the alcoholic extraction still contains the major portion of the antirachitic and antiophthalmic vitamines originally present.

The acid extract is both antirachitic and antiophthalmic. The residual oil, after acid extraction, is no longer active. In other words, the acid has extracted the active principles of the oil.

The concentrate made by means of these acid extractions followed by saponification contains the antiophthalmic and antirachitic vitamines; therefore, this particular process is an advantage in that we have been able to extract both vitamines.

As regards the statement of Dr. Wood that the concentrate does not represent all of the therapeutic value of the cod liver oil, I feel that it is not valid, for this reason: The activity of the oil at one time was attributed to its nitrogen or phosphorus content. This has been disproven because the concentrate contains neither nitrogen nor phosphorus; and yet if it is mixed with sugar, for example, the therapeutic activity of the mixture is exactly the same as that of fresh cod liver oil. In other words, the oil has been replaced by sugar but the therapeutic effect is the same because of the presence of the concentrate.

The oil remaining after acid extraction is no longer effective in those nutritive disturbances for which cod liver oil is used. In view of the foregoing, we are justified in saying that the therapeutic value of cod liver oil, as far as experimental evidence is concerned, is due to its vitamine content.

As regards the stability, we have found that the product is stable even after seven or eight months, so far. As long as the concentrate is protected against oxidation, there is no loss of activity. This is assured by carrying out the process in a non-oxidizing atmosphere.

As to the details of manufacture, they are largely given in the detailed paper to be published shortly in the *Journal of Metabolic Research*.

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DIETHYLPHTHALATE III.*

BY J. A. HANDY AND L. F. HOYT.

1. INTRODUCTION.

A survey of the data on diethylphthalate appearing since our last paper on this subject (1) and a study of some recently proposed detection tests, have been made.

2. METHODS OF DETECTION.

A detection test for diethylphthalate involving the use of pyrogallol, quite different in its results from the fluorescein type test or the phenolphthalein test of Calvert, has been proposed by Eilles (2). This author deprecates the use of phenol-H_2SO_4 (*i. e.*, the Calvert Test) as being of little use (no reasons given) and states that the resorcinol- H_2SO_4 tests, (*i. e.*, like those of Lyons, Handy and Hoyt, and Andrew) are uncertain because of fluorescence in blanks. The Eilles test, which is official at the German Bureau of Internal Revenue (Hamburg) is carried out as follows:

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* Scientific Section, A. PH. A., Buffalo meeting, 1924.

(1) In the case of spirits 20 to 50 cc. of sample to which are added 5 drops of a 15% solution of sodium hydroxide, are evaporated on the steam-bath in a flat porcelain dish.

(2) In the case of liquors which contain sugar, or extractive matter and other substances, particularly formic acid, 20 to 50 cc. of sample are diluted with an equal volume of water and shaken out with 25 cc. of petroleum ether (30–50° b. p.). Tinctures (extracts of drugs) are treated with the necessary amount of lead acetate and filtered before extraction. Petroleum ether extract is evaporated in a flat porcelain dish without the addition of caustic soda.

The evaporated residues from (1) and (2) are mixed with 5 to 10 drops of 1.84 H_2SO_4 with the aid of a glass stirring rod and heated over a small flame with continuous stirring, until the fumes of the acid begin to be given off. Then the dish is heated somewhat more strongly at the spot where the pyrogallol is to be applied, in order that the pyrogallol will melt immediately. By tilting the dish the sulphuric acid is allowed to flow away somewhat and a few crystals of pyrogallol are immediately placed on the heated spot. In the presence of diethylphthalate a genuine violet-red color is immediately produced.

The test has been severely criticized in Germany. Wewers (3) claims that blank tests made on alcohol of known purity and even blanks with the reagents only, all gave a violet-red color. Wewers prefers to rely on the sense of taste for detection of diethylphthalate, which taste is pronounced even in high dilutions, although he gives no quantitative data.

Note: We have previously pointed out (JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 13, p. 607) that 0.1% diethylphthalate can be easily detected in miscellaneous beverages by the sense of taste.

Utz (4) likewise finds the official German method faulty. Other colors whose interpretation is doubtful are liable to be produced. Formic acid, against the presence of which Eilles warns as giving a reaction very similar to diethylphthalate, was found by Utz to give more of a brick-red, which would not be mistaken for the color produced by the ester.

Utz proposes a modification of Lyons method in which he eliminates the use of caustic soda and heats a 1-cc. sample (of spirits, or of samples free from appreciable amounts of interfering substances) with 1 cc. 1.84 H_2SO_4 until white fumes of the acid appear. A few crystals of resorcinol are then added and the mixture is heated until it turns brownish red, cooled and poured into 500 cc. water made alkaline with ammonia.

Leffman (4) reports his experience with the Utz method, which he finds simpler and quicker than methods previously suggested. This author states, however, that although the Utz method will detect very small amounts of diethylphthalate, it gives positive "blank" tests which are apt to be misleading. Good results were obtained in the presence of commercial methanol and reasonable amounts of isopropyl alcohol, though an excess of the latter tended to obscure the result.

Leffmann recommends Andrew's Method (6) as simple and dependable, satisfactory results being obtained on 2 milligrams of diethylphthalate in the presence of small amounts of acetaldehyde and commercial methanol and isopropyl alcohol.

3. Fluorescence Phenomena.

Considerable data has appeared in the recent literature concerning the fluorescence of fluorescein and analogous compounds. In our second paper (Journal of the American Pharmaceutical Association 13, p. 606) we stated that possibly the examination of the absorption spectra of genuine fluorescein and that of the resorcinol-saccharin compound, *i. e.*, sulphonefluorescein, so similar to the naked eye, might show differences. Orndorff and Vose (7) have reported just such an expected difference. They examined the absorption spectra of true fluorescein and that of sulphonefluorescein (which they prepared in the pure crystalline condition from several compounds including saccharin). Both compounds in equal dilutions, which could scarcely be differentiated with the naked eye, showed single absorption bands but with different maxima, that of sulphonefluorescein lying at $\lambda = 5249$ and being 10% more intense than that of fluorescein lying at $\lambda = 5209$.

Additional data on the tendency of products made by condensation with resorcinol to exhibit fluorescence in alkaline solution is furnished by Sen and Sinha (8). These investigators condensed resorcinol with a number of aldehydes and among others report the following, listed in Table I.

Table I.

Resorcinol condensed with	Color of product. In conc. H_2SO_4.	In alkaline solution.
Benzaldehyde	Orange	Red with red-green fluorescence
Salicylic Aldehyde	....	Orange with red-blue fluorescence
Vanillin	Pink	Red-violet with green fluorescence
Chloral Hydrate	Yellow	Red with red-green fluorescence
Furfurole	Orange	Red with red-green fluorescence
Anisaldehyde	Dark red	Red with bluish fluorescence
Paraldehyde	....	Red with red-green fluorescence

They noted that the substitution of the trihydric phenol, pyrogallol, for resorcinol in condensation experiments with benzaldehyde gave a product devoid of fluorescence in alkaline solution.

4. Miscellaneous Data on Diethylphthalate.

Utz makes some interesting observations on diethylphthalate. It appears that the authorization of this denaturant in Germany on May 12, 1922 in the proportion of 2 volumes per 100 volumes of alcohol (subsequently reduced on Jan. 19, 1923 to 1 volume per 100) was followed quickly by complaints and hesitancy in its use. According to Utz it was claimed by Dr. Payr, director of the surgical clinic at Leipzig, that alcohol denatured with (2%) diethylphthalate irritated the skin, which it reddened with a burning, itching sensation and caused it to become rough and scaly. He stated further that it produced a numbing sensation in the finger tips.

The German Druggists Association applied to the German Health Office for a ruling in regard to the use of Alcohol denatured with diethylphthalate in cosmetics. In reply (*Pharm. Ztg.*, 68, 643 (1923)) the association was assured that the ester could be used without risk, in the quantities in which it was added to denatured alcohol, in toilet waters and preparations for external use.

Utz mentions the use of diethylphthalate as an adulterant, reported by Schimmel as being found by them in Oil of Rose and Oil of Lavender. He further states

that the ester is better known perhaps on account of its war uses, among which was its employment as a glycerin substitute by the German Army in filling the heating jackets of field kitchens.

5. Experimental Part: Methods of Detection.

(A) Eilles pyrogallol test.

This test was applied to diethylphthalate and to a number of other compounds. In our experience this Official German Test for Diethylphthalate was found to be of little or no value for the following reasons:

1. The intensity and duration of the color reaction vary according to the degree of heat applied.

2. Impossible to standardize the procedure so that different operators can consistently get the same result.

3. Not sufficiently characteristic for diethylphthalate.

(*a*) Blanks are highly colored and of a bluish violet quite similar to the reddish violet produced with diethylphthalate.

(*b*) Saccharin and Vanillin were found to give a test with pyrogallol indistinguishable from that produced with diethylphthalate.

(*c*) Other substances such as succinic and formic acids, as well as chloral hydrate, give similar and confusing color reactions.

4. At best the test is very fugitive and fades quickly to a brown. Unless the test is carried out very carefully the color reaction is liable to be obscured by the charring or blackening of the reagent.

5. Less sensitive than the fluorescein type test.

Some experiments were made on the effect of substituting other phenols for pyrogallol in the Eilles test. The procedure was as follows:

Five drops 1.84 H_2SO_4 were heated in a small porcelain capsule *until white fumes of the acid appeared*. Then a few fragments of the phenol under consideration were applied to the heated area and the color reaction noted. All of the phenols tried give a bewildering series of color changes in blank tests, as follows:

	Reagent.	Colors in blank test.
(1)	(Mono.) Phenol	Amber, reddish brown, dark brown
(2)	(di.) Hydroquinone	Rose, reddish violet, brown, dark green
(3)	(di.) Resorcinol	Yellow, orange, olive-green
(4)	(tri.) Pyrogallol	Rose, reddish violet, blue-violet
(5)	(tri.) Phloroglucinol	Deep yellow, orange, olive-green
(6)	α-Napthol	Red-brown, surrounded by a bright lavender ring
(7)	β-Napthol	Brown, brownish green

The reaction mixtures were poured into dilute alkali. No. 3 Resorcinol showed a green fluorescence, No. 7 β-Napthol a greenish blue fluorescence, the others no fluorescence.

Such intense and fugitive colors were obtained in these blank tests that it was considered a waste of time to continue experiments with a test of this type.

(B) Reaction between various phenols, and certain aromatic and aliphatic compounds.

A systematic study was made of the possibility that some phenol other than resorcinol could be used to better advantage in the detection of diethylphthalate,

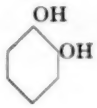
by formation of a condensation product rather than a spot color test. In order that conditions should be as uniform as possible, the procedure of heating for 3 minutes in an oil-bath at 160° C. was adopted. In addition to a blank test and a test on diethylphthalate, we applied the same procedure, at the same time, to a number of other substances which we, or others, have found to condense with resorcinol to form compounds showing fluorescence in alkaline solution.

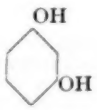
The available phenols and the substances with which they were condensed are listed in Table II.

TABLE II.

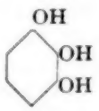
A. Phenols.

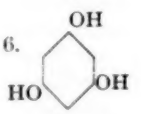
1. Phenol

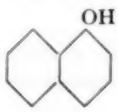
2.  Catechol (o)

3.  Resorcinol (m)

4. Hydroquinone (p)

5.  Pyrogallol (1–2–3)

6.  Phloroglucinol (1–3–5)

7.  α-Napthol

8. β-Napthol

B. Substances tested.

1. Diethylphthalate
2. Acetone
3. Anisaldehyde
4. Benzaldehyde
5. Chloral Hydrate
6. Formic Acid
7. Malic Acid
8. Saccharin
9. Salicylaldehyde
10. Succinic Acid
11. Vanillin

The procedure was as follows:

0.05 gram of each phenol, 0.05 Gm. or 1 drop of each substance (if liquid) to be tested and 1 cc. 1.84 H_2SO_4 were placed in hard glass test-tubes and the tubes heated for 3 minutes in an oil-bath maintained at 160° C. After cooling the reaction mixtures were added to 100 cc. of a 5% solution of NaOH and the color and fluorescence noted. (It is quite probable that in some cases no condensation took place under the above conditions of concentration and temperature, but this

is of little importance in this investigation, since we are concerned only in comparing reactions of diethylphthalate and other substances under identical conditions.)

A blank test was, of course, made on each of the phenols. None of these series of tests afforded a method of detection equal to the fluorescein test, *i. e.*, condensation with resorcinol. The intensity and brilliance of fluorescein, and particularly its permanence, are much greater than in the case of any of the condensation products from equal weights of substances (particularly formic acid, saccharin, and succinic acid), reacting in a similar manner with resorcinol.

To study the effect of temperature, the condensation with each of the phenols and diethylphthalate was also made at a higher temperature.

The colors of the final alkaline solution of the blanks and of the condensation products of diethylphthalate with the several phenols are recorded as Table III.

Procedure: A. 0.05 Gm. each of the phenols and diethylphthalate, 1 cc. 1.84 H_2SO_4, heated together for 3 min. at 160° C.

Procedure: B. 0.05. Gm each of the phenols and diethylphthalate, 12 drops 1.84 H_2SO_4, heated over a free flame until fumes of the acid started to appear (*i. e.*, procedure like the Calvert Test).

TABLE III.

	Procedure A, Color in alkaline solution.		Procedure B, Color in alkaline solution.	
	Blank.	Test with diethylphthalate.	Blank.	Test with diethylphthalate.
Phenol	Colorless	[1]Colorless	Colorless	Pink
Catechol	Bright yellow	Bright yellow	Greenish yellow	Dark brown
Resorcinol	Colorless	Yellow with intense greenish fluorescence	Colorless	Reddish brown, green fluorescence
Hydroquinone	Pale olive-green, bluish fluorescence	Light brown with bluish fluorescence	Amber	Purplish brown
Pyrogallol	Greenish yellow	Yellowish green	Olive-green	Olive-green
Phloroglucinol	Amber	Brownish red	Amber	Reddish brown
α-Napthol	Pale amber	Amber	Pale amber	Light brown, bluish fluorescence
β-Napthol	Pale greenish yellow, green fluorescence	Exactly like blank, same degree of fluorescence	Brown, green fluorescence	Brown, green fluorescence

[1] Condensation to form phenolphthalein does not take place apparently at 160° C. under the conditions of our test. A higher temperature, as in the Calvert test, appears to be necessary.

It will be noted that procedure B, which was tried with the various phenols and diethylphthalate only, heating at a higher temperature than A, tended to produce deeper colored final solutions.

In the course of the series of tests made according to procedure A with each of the 8 phenols and 11 substances listed in Table II, two outstanding facts were observed, *viz.:*

(1) The fact that some phenols give rise to condensation products which are fluorescent in alkaline solution whereas other phenols do not.

Classification of Phenols with regard to the fluorescence, or lack of it, shown in alkaline solution by the condensation products made by heating 0.05 Gm. of a

phenol (column A, Table II), with 0.05 Gm. of certain substances (column B, Table II) and 1 cc. 1.84 H_2SO_4 for 3 min. at 160° C., is tabulated in Table IV.

TABLE IV.

Phenols whose condensation products are fluorescent in alkaline solution.	Phenols whose condensation products show no fluorescence in alkaline solution.
Resorcinol—Green Fluorescence	Phenol
Hydroquinone—Blue Fluorescence	Catechol
β-Napthol—Blue Fluorescence	Pyrogallol
	Phloroglucinol
	α-Napthol

With resorcinol, hydroquinone, and β-napthol, all of the final test solutions from the 11 reacting substances showed fluorescence of varying intensity, but unmistakable in all cases.

(2) A remarkable parallelism was found to exist in the appearance, *i. e.*, as regards color and fluorescence or lack of it, of the final alkaline solutions of the condensation products of diethylphthalate, formic acid, saccharin, and succinic acid with each of the phenolic substances of column A, Table II. This data supplements and elaborates the data previously reported in our second paper under part II B (4) "Fluorescent Phenomena and color reactions resulting from condensation of resorcinol and phenol with substances other than phthalic acid derivatives."

While acetone, chloral hydrate, and the various aldehydes gave in general dark brown, red, or purple in the final test solutions throughout the series, the above four similarly reacting substances gave in general clear light-colored solutions.

(C) COMPARISON OF THE SENSITIVENESS OF THE FLUORESCEIN TESTS FOR DIETHYLPHTHALATE OF UTZ, ANDREW, AND HANDY-HOYT.

Each test was carried out carefully according to its specific directions on 0.2 mgms. and 10 mgms. of diethylphthalate in 1 cc. absolute ethyl alcohol. Results are shown in Table V.

TABLE V.

	A, Utz.	B, Andrew.	C, Handy-Hoyt.
Blank (1 cc. absolute ethyl alcohol)	Reddish brown strong fluorescence	Colorless	Colorless
1 cc. absolute ethyl alcohol and 0.2 mgm. diethylphthalate	Solution less red than blank. Strong fluorescence	Faint fluorescence	Distinct—stronger than B
1 cc. absolute ethyl alcohol and 10 mgms. diethylphthalate. (Equivalent to 1 cc. 39-C Spec. Den. Alcohol, 1% diethylphthalate).	Solution dark amber. Intense fluorescence	Intense yellow-green fluorescence	Intense yellow-green fluorescence

Due to the high temperature employed in the Utz test, a strongly positive blank is, in our opinion, unavoidable, and renders this test of little value in detecting traces of diethylphthalate. In the above tests the fluorescence of the blank was greater when fresh than that with 0.2 mgm. diethylphthalate.

The Andrew test, we belive, is rightly regarded by all who have tried it as a very satisfactory test, convenient, rapid, and sensitive; although our experience has been

that the maximum amount of fluorescein is not produced at the moderate temperature employed and that the fluorescence is correspondingly less intense than that obtained on the same weight of diethylphthalate in a test like our own made at 160° C. The Andrew Test is the least liable to give positive "blanks," because of the very moderate condensation temperature employed.

We would again point out that the matter of positive blanks may be due primarily, to (1) too high a temperature, especially if part of the resorcinol remains undissolved in the acid and exposed to the air on the sides of the dish or tube during the condensation. (2) Impurities of various kinds in the sample under test. In this connection we have repeatedly obtained blanks entirely devoid of fluorescence when working with absolute or otherwise specially purified ethyl alcohol, by both the Andrew Test and our own, and have likewise obtained temporarily positive blanks by both methods on commercial alcohols free from diethylphthalate.

(D) USE OF DILUTE H_2SO_4 IN PETROLEUM ETHER EXTRACTION OF DIETHYLPHTHALATE.

Comparison of extractions with petroleum ether from solutions diluted (1) with water and (2) with dilute H_2SO_4 (10%).

A small quantity of "39-C." was made in the laboratory, using 50 cc. Absolute Alcohol and 0.50 cc. Diethylphthalate.

1. *Gravimetric Test.*—In order to secure weighable quantities of the ester, extractions were made under the following conditions.

	Extraction from: Aqueous solution.	Dilute H_2SO_4.
Test solution of the ester		
5 cc. Dist. H_2O		
4 cc. Absolute Alcohol		
1 cc. 39-C.	10 cc.	10 cc.
Added Liquid	10 cc. (H_2O)	10 cc. (10% H_2SO_4)
Petroleum Ether	20 cc.	20 cc.
Theoretical weight of diethylphthalate	0.0111 Gm.	0.0111 Gm.
Wt. of ester recovered in petroleum ether extract	0.0104 Gm.	0.0105 Gm.

Both extractions were shaken 20 times in the same manner in separatory funnels and allowed to stand over night. In the above test the concentration of diethylphthalate in the original 10 cc. test portion is 0.1%, and 0.05% after dilution with the added liquid. The concentration of alcohol in the final liquid under extraction was 25% by volume.

2. *Qualitative Test.*—Effect of concentration of alcohol, and acid on the extraction of minute amounts of the ester in qualitative tests.

(A) Extraction of a 10 cc. portion of a sample containing 10% by volume of alcohol (comparable to sweet wine) and 0.01% of diethylphthalate after dilution with (1) water, and (2) dilute H_2SO_4.

	1.	2.
Ester	1 mgm.	1 mgm.
Alcohol	1 cc.	1 cc.
Water	9 cc.	9 cc.
Added Liquid	10 cc. Water	10 cc. H_2SO_4 (10%)
Petroleum Ether used	20 cc.	20 cc.
Fluorescein test on extract	+++	++

Note: Extraction from aqueous solution gave in this case a fluorescence of greater intensity than was obtained on the strictly parallel extraction from dilute H_2SO_4.

(B) Extraction of a 10 cc. portion of a sample containing 50% by volume of alcohol (comparable to whisky, brandy, or gin) and 0.01% of diethylphthalate after dilution with (1) water, and (2) dilute H_2SO_4.

	1.	2.
Ester	1 mgm.	1 mgm.
Alcohol	5 cc.	5 cc.
Water	5 cc.	5 cc.
Added Liquid	10 cc. Water	10 cc. H_2SO_4 (10%)
Petroleum Ether used	20 cc.	20 cc.
Fluorescein test on extract	+	++

Note: Extraction from acid solution gave in this case the stronger fluorescein reaction.

Summary.

1. Extraction of 10 cc. of an alcoholic sample containing a ponderable amount (*i. e.*, 0.1%) of diethylphthalate with petroleum ether effects the same high percentage of recovery of the ester, irrespective of whether the sample is diluted with equal volumes of water or 10% sulphuric acid.

2. Qualitative fluorescein tests on the petroleum ether extracts of 10 cc. samples containing 1 mgm. (0.01%) of the ester show no consistent superiority of dilution of the sample with 10% sulphuric acid. Results are variable; several tests for the ester in beverages as well as in solutions of the ester in pure absolute alcohol show sometimes a more intense fluorescein reaction on extracts from an aqueous medium and at other times a superiority in favor of extraction from an acid medium.

3. Due, however, to the beneficial effect of the acid in preventing the formation of emulsions during extraction, its use is recommended. Samples to be extracted should then be preferably diluted with an equal volume of 10% sulphuric acid in place of water.

4. The fact that 10 mgm. diethylphthalate can be extracted nearly quantitatively from a solution whose total volume is 20 cc. and whose alcoholic content is 25% by volume, does not mean that 1 mgm. can be extracted to a like extent from an entirely similar solution. The intensity of fluorescein tests on such extractions of solutions containing 1 mgm. of the ester is much less than that of a blank of 1 mgm. of the ester.

Official U. S. Treasury Department Test for Diethylphthalate.

The Bureau of Internal Revenue of the U. S. Treasury Department employ as their official test for diethylphthalate a procedure which combines the essential features of both the Andrew method and our own. Details of this official method, furnished by Dr. J. M. Doran, Head, Industrial Alcohol and Chemical Division, Bureau of Internal Revenue, Washington, D. C., are as follows:

"A. FOR LIQUIDS OR SOLUTIONS CONTAINING A CONSIDERABLE AMOUNT OF DIETHYLPHTHALATE.

"To 10 cc. of the sample add 2 cc. of a 10% solution of sodium hydroxide and evaporate to complete dryness on the steam-bath. Add about 5 cc. of concentrated sulphuric acid and 25 milligrams of resorcin and heat for five minutes on the steam-bath. Transfer the contents to a test-tube and heat for about 5 minutes to 160° C. in a paraffin bath. Cool. Pour contents into about 300 cc. of water and make alkaline with strong sodium hydroxide solution. The presence of diethylphthalate (in the absence of other phthalates) is indicated by the greenish yellow fluorescence of fluorescein."

"B. FOR LIQUIDS OR SOLUTIONS CONTAINING A TRACE OF DIETHYLPHTHALATE.

"To not less than 50 cc. (preferably more) of the sample add 0.2 cc. of a 10% solution of sodium hydroxide and evaporate to dryness on steam-bath. Add about 5 cc. concentrated sulphuric acid and 25 milligrams of resorcin and heat for about 5 minutes on the steam-bath. Transfer the contents to a test-tube and heat for about five minutes to 160° C. in a paraffin bath. Cool. Pour contents into about 150 cc. of water and make alkaline with strong sodium hydroxide solution. Allow to stand about 24 hours. A greenish yellow fluorescence of medium intensity when the solution is viewed through the long axis of a Nessler's tube is indicative of diethylphthalate.

"*Note:* A blank test on pure alcohol should be made for comparison. Final alkaline solution should always be allowed to stand for 24 hours before making decision, since fluorescence is always produced, even in the blank. In the absence of diethylphthalate, this fluorescence will entirely fade away upon standing the required length of time. All apparatus should be thoroughly cleaned, since any phthalate will respond to this test."

Attention is called to the fact that this official method recognizes the necessity of interpreting results 24 hours or more after the tests have been made A similar caution was inserted in our second paper, Diethylphthalate II (p. 706).

It is understood of course that any fluorescein-type test for diethylphthalate is to be applied directly only to samples free from interfering substances and that a preliminary extraction with petroleum ether is advisable if the sample contains sugars, extractive principles of drugs, and other interfering substances. The test is positive only for the phthalic radical.

General Conclusions.

1. The official German test for diethylphthalate, employing pyrogallol, is of very little value. Substitution of other phenols for pyrogallol is of no advantage.

2. The Utz fluorescein-type test is unsatisfactory because the high temperature employed gives rise to positive blanks showing strong and persistent fluorescence.

3. For all practical purposes the Andrew Test combines a sufficient degree of sensitiveness with rapidity and convenience. In general it is the least troublesome of the fluorescein type tests as regards "blanks."

4. In our opinion the most comprehensive and refined test so far developed is the one now in use by Internal Revenue Dept. This method combines the

essential features of the Andrew Test with a supplementary heating at 160° C. whereby the yield of fluorescein is increased, which tends of course to increase the sensitiveness of the test. In addition this test includes the caution of interpreting results on traces of diethylphthalate after the test solutions have stood at least 24 hours.

ABSTRACT OF DISCUSSION.

James M. Doran said that Mr. Handy was a little over-modest in his last statement, about the test being developed in the Laboratory of the Internal Revenue Department. Part of the work had been done there, but most valuable help was given by Mr. Handy and, in his opinion, most of the credit for the present development of this test is due Mr. Handy and his laboratory. He said further, in substance, that the test has entered largely into the work of the chemists of the Revenue Department, because an attempt is necessary to fix the purity of alcoholic samples taken by agents. It gives some clue or inference as to the possible source of alcohol of questionable nature. It is of considerable importance to pharmacists and the chemists of the Revenue Department would be very glad to see a little more work done on this and other denaturants; thereby great protection would be given pharmacists. The necessity of reliable qualitative tests is obvious; not only does the Department want to be assured of the quality of alcohols that may be used, but also that the tests do not lead to erroneous conclusions. The inferences that might be drawn from finding diethylphthalate in certain samples of alcohol, in the possession of pharmacists, might be unjust and embarrass them; the Department is desirous that these tests be developed so they can be used with assurance.

D. M. Copley said that, in his experience, these products are now nearly odorless; formerly they had a pleasant aromatic odor.

The author replied that they had samples of nearly all diethylphthalates, of commercial consequence, manufactured here and abroad. There is much interest in the subject and many samples are submitted to them for an opinion. Diethylphthalate when made from pure basic products has a slight odor; formerly, some manufacturers added a perfume oil to cover up this odor.

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NEW VETERANS' HOSPITAL.

Construction of a general hospital for war veterans near the Twin Cities or Rochester, Minn., has been approved by President Coolidge.

Plans for the hospital, as drawn up by the Federal Board of Hospitalization, included provision for an observation ward for tubercular patients.

Present hospital facilities at Hot Springs, S. D., will be extended to accommodate 300 more tuberculosis patients.

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THE INERT GASES OF THE ATMOSPHERE.*

BY WYATT W. RANDALL.[1]

I.

In the case of any classical research, interest in the mental processes of the investigators as they worked upon the material which was available, may long outlast that in the actual facts brought to light. These last are soon absorbed into the great mass of scientific data stored in works of reference and the romance of their discovery is in large measure lost to the average student. Hence it is most desirable that what may be called their anecdotal history should be preserved and should be available to inspire those who are seeking to enlarge the domain over which exact science maintains its sway. The average school boy of to-day can tell you facts concerning the atmosphere which were not even suspected by the most profound student of chemistry thirty-five years ago, yet it may safely be predicted that, two hundred years from now, the investigations conducted by Lord Rayleigh and Professor Ramsay will continue to stimulate, and to awaken admiration in, the chemist of that time.

In his efforts to secure the greatest attainable accuracy in the determination of the weight (under standard conditions of temperature and pressure) of a liter of each of the lighter elementary gases, Lord Rayleigh strove to avoid any possible source of error: (*a*) in the production of pure samples; (*b*) in the determination of the temperature and pressure at the time of filling his glass container; (*c*) in the weighings; (*d*) in determining the volume of the container. The ingenious devices employed to secure one or other of these ends cannot be discussed at length here. Most important of all was the decision to prepare samples of each gas by at least two different methods, in order to avoid the introduction of a constant source of error. This decision led to the discovery of the inert gases of the atmosphere: for, after a satisfactory series of weighings had been made with "nitrogen" secured by the removal of all other known constituents from air, he followed this up with another series in which the gas had been produced by passing a mixture of air and ammonia through a hot tube. The density of the latter gas was about 1/1000th lighter than atmospheric "nitrogen." Experiments of various kinds failed to show the presence of any impurity in this "chemical nitrogen." Instead of assuming that some annoying and probably undiscoverable source of error vitiated his later results, and letting it go at that, Lord Rayleigh doggedly set to work to *increase*, if possible, the discrepancy observed. He prepared nitrogen from pure oxygen and ammonia: this would contain no atmospheric nitrogen. The discrepancy between the density figures of atmospheric "nitrogen" and "chemical" nitrogen was found to be now 6–7 times as great as before. Suspicion, therefore, began to involve the atmospheric "nitrogen," in spite of the fact that all previous researches, as well as that now in hand, had been based upon the (apparently safe) assumption that pure nitrogen was obtained when dry air, free from carbon dioxide, had been

* This paper is a summary of an address delivered before the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION on January 27, 1925.

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caused to pass repeatedly through a tube filled with red-hot copper filings. Lord Rayleigh now prepared atmospheric "nitrogen" by the use (*a*) of iron filings and (*b*) of ferrous hydroxide, in the place of copper. The gas obtained in each case exhibited the same density as did that obtained from the air with the aid of copper.

Was the trouble after all with the "ammonia nitrogen?" He prepared "chemical nitrogen:" (*a*) from nitric oxide, (*b*) from nitrous oxide, (*c*) from urea, (*d*) from ammonium nitrite purified by two different methods: in each case practically the same results were obtained as with "ammonia nitrogen:" not only did the discrepancy remain, but it was constant in amount.

Lord Rayleigh's attention was now called to an experiment performed by Cavendish about 115 years before, in which a stream of sparks from a frictional electric machine had been sent through a quantity of air mixed with pure oxygen and contained in a glass tube over mercury. After removal of excess oxygen and of gases soluble in alkali solution, Cavendish had found there was a small bubble of gas remaining which refused to yield to the action of his agents. Lord Rayleigh, therefore, set to work to repeat Cavendish's experiment on a large scale and, at the same time, suggested to Professor Ramsay that he, too, endeavor to solve the problem which the nitrogen results had shown to exist.

The outcome is well known. Lord Rayleigh, by the prolonged action of an electric arc upon a mixture of air and oxygen contained in a large vessel over strong soda solution; and Ramsay, by passing purified air repeatedly over hot magnesium contained in a glass tube; succeeded (1894) in removing from air all its constituents known up to that time: about 1% of the original volume of the air remained, and to this residue they gave the name of "argon," the inert one.

From this point on, the interest centers chiefly about the work of Ramsay. The density of the new gas was determined with great care and its spectrum was mapped. The ratio of its specific heats, its behavior towards reagents, its coefficient of expansion with heat, etc., showed that it was monatomic, with no capacity to form compounds. Search for possible compounds led Ramsay (1895) to examine a gas—supposedly nitrogen—given off from certain rare minerals under the influence of high temperature. After purification from known constituents, spectrum examination showed that this gas was not argon, but a new inert element whose presence in the sun's higher atmosphere had been detected 25 years before and which now was shown to be present in minute quantity on the earth—helium.

Prolonged study of the behavior of helium and argon led to the conclusion that the former has an atomic weight of nearly 4—following hydrogen and preceding lithium in the Periodic System—and that the latter has an atomic weight of nearly 40, thus following chlorine and preceding potassium in the Table. Ramsay argued that if an inert gas comes just after chlorine, there ought to be one just after fluorine, another just after bromine, another just after iodine. Similarly, if one is known which precedes lithium and another which apparently precedes potassium, there ought to be one to precede sodium, one to precede rubidium and one to precede caesium. In other words, are there inert, monatomic gases whose atomic weights are approximately 20, 82 and 128, respectively? And where should one expect to find them? Might not argon, after all, turn out to be a mixture?

This last question had frequently been asked, for the density of argon pointed

to an atomic weight (39.92) higher than that of potassium, whereas its properties showed that its place in the Periodic System is evidently before potassium. If argon is a mixture, it might consist of a chief constituent, say, of atomic weight 38 and of one or more heavier gases (in small quantity) which would raise the average density to 20, as compared with that of hydrogen taken as unity. Moreover, certain lines in the helium spectrum coincided with lines in the argon spectrum: this suggested the presence of a common constituent. But if argon is a mixture of *inert* gases, how can they be separated from one another? Chemical methods would obviously be of no avail. Ramsay attacked the problem from two directions: making use of (1) assumed differences in density, and (2) assumed differences in volatility.

The details of this experimental work cannot be gone into here. Suffice it to say that, by the use of boiling liquid air as a cooling agent, a lighter fraction was separated from argon, and this in turn, by the use of *boiling liquid hydrogen*, was separated into helium (which was under these conditions still a gas) and a (liquefied) new gas, neon, whose density was half that of argon and its atomic weight therefore 20. The first of the gases looked for had been found!

Various facts led to the conclusion that if heavier constituents exist in what had been called argon, they must be present in very small quantity. Obviously their separation in a reasonably pure form would thus be a matter of extreme difficulty; nevertheless it was done. By *fractional distillation* of liquefied argon, and separation and redistillation of the several fractions obtained—the process being repeated again and again—it was ultimately possible to separate and purify two heavier gases; krypton, with an atomic weight of 81.56, and xenon, with an atomic weight of 128.0. All the gases sought had been isolated, and each fitted perfectly into its place in the Table!

Some idea of the difficulties involved in this work can be gained if one bear in mind the relative amount of each of these gases in the atmosphere. In twenty million volumes of air there are contained about:

187,400 volumes of argon	30 volumes of helium
300 volumes of neon	20 volumes of krypton
1 volume of xenon	

Various physical constants were determined for each of these gases in turn. And yet Ramsay had only a little over 2 cc. of gaseous xenon to work with!

The discovery of krypton and xenon has not solved the problem of the atomic weight of argon; this seems to be approximately 39.96 and therefore distinctly greater than that of potassium.

II.

Let me now turn to an informal discussion of some of the details of technique which, to me at least, were a source of intense interest. And let me begin by saying that I am relying in large measure upon my memory, for by no means were all these devices, so far as I can recall, described in print.

(1) The method employed by Lord Rayleigh in determining the relative densities of the several elementary gases and their several weights per liter under standard conditions, was only a modification of that which had been used by

Regnault, von Jolly, Leduc, Cooke, and others. It consisted essentially in weighing a glass balloon provided with a tap, (*a*) when vacuous and (*b*) when filled at a known temperature and pressure with each of the gases in turn. The capacity of the balloon up to and including the bore of the tap, was approximately 1836 cc.; this was determined by filling it with water at 0° C. and weighing it in a room whose temperature was close to 6° C.; under these conditions there was no overflow from the tap.

(2) The buoyant effect of the air upon the globe at the time of a weighing had to be determined with great care. It was found that the globe when vacuous was smaller by an appreciable amount than when filled with gas at approximately atmospheric pressure; this was allowed for in the calculations.

(3) One of the most formidable difficulties connected with work of this kind is that due to atmospheric moisture deposited upon the glass balloon and so adding an indeterminate amount to its weight. Many investigators have attempted to overcome this difficulty by drying as completely as possible the air in which the balloon was hung while the weighing was in progress—in other words, the balloon was suspended in a desiccator prior to and during the weighing. Lord Rayleigh saw that if a *constant* hygroscopic condition could be maintained in the balance room, it made no difference how much moisture was deposited on the balloon: if it were a constant amount, it would be weighed each time as was the glass of the balloon itself. Accordingly, prior to each series of weighings, he hung around the balance room a row of blankets which had been baked in an oven; in a comparatively short time equilibrium was established between the atmosphere and the blankets and—which is the important thing—the hygroscopic state of the air in the room was the same, day after day, whatever it might be in the open.

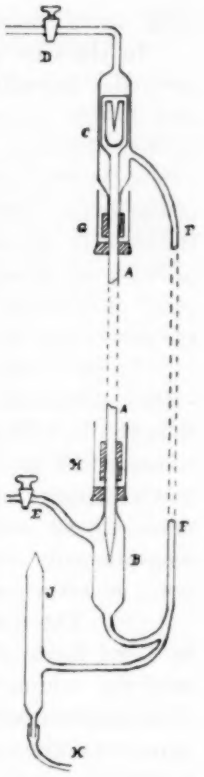
(4) It goes without saying that, in weighings where a hundredth of a milligram plays a part of some importance, the presence of a person close to the balance may cause an appreciable error. To avoid an error of this sort, Lord Rayleigh made it a practice to suspend the balloon from the balance, to adjust the weights, to arrange the blankets in position, to start the balance swinging, to close the room and—as this was done in the evening—then to go to bed. In the morning, from another room a beam of light was thrown on the balance-scale and, by means of a telescope set in the wall, the swings of the pointer were noted.

(5) The balloon was always surrounded by melting ice at the time of filling; temperature control was therefore easily secured. The exact determination of the pressure exerted upon the gas inside the balloon was, however, a difficult matter. Lord Rayleigh solved this difficulty in characteristic fashion: instead of referring the filling pressure to the barometric height at the time, he made use of a manometer and always filled the balloon at the same pressure; this called for but one pressure adjustment and removed all fear of inaccurate barometric readings due to varying meniscus form. A stout iron rod, provided at each end with a sharp point turned down, was enclosed in the manometer in such a way that the upper point was close to the mercury surface in a chamber connected with the air-pump, while the lower point was close to the mercury surface in a chamber connected with the glass balloon; the glass tube through which connection was established between the mercury in the upper chamber and that in the lower, was, like the chambers themselves, protected by insulating material. The temperature of the mercury

was noted. When each point was brought, by adjusting the mercury reservoir, to coincide with its reflection in the mercury surface, the gas in the balloon was under a pressure corresponding to that of a mercury column equal in vertical height to the distance between the two points on the iron rod. The vacuum in the upper chamber could be tested at any time by means of the pump; proper precautions eliminated any possibility of an error due to changing length in the iron rod. The exact length of the latter, between the two points, having been determined once for all—it was a little over 762 mm.—all pressure measurements could be reduced to terms of standard pressure at 45° latitude.

(6) I cannot forbear introducing a reference to Lord Rayleigh's Töppler pump. When I first went to work in his laboratory, it fell to me to transfer a quantity of (at that time) most precious helium which I had brought from London, from a sealed glass container to his interferometer. One look at the pump appalled me, and my concern filled him with amusement. It turned out that, two years before, someone, in handling the pump carelessly, had allowed mercury (with atmospheric pressure behind it) suddenly to enter the vacuous bulb—with the result that a hole the size of a half-dollar had been knocked in the side. On examination, however, he had found that a single piece of glass had been broken out, that this had not been chipped, that there were no cracks in the bulb and that the piece would stay in its place if put back and held by pressure from outside! The pump was needed at once; to secure a new bulb and install it would have caused several days' delay; so Lord Rayleigh had caught up a lot of old examination papers, had tied them like a cornucopia around the bulb of the pump and, after restoring the piece of glass exactly to its place, had filled the cornucopia with mercury until the damaged part of the bulb had been drowned in a mercury seal. The paper cornucopia was begrimed with dust and the mercury it contained was hardly recognizable. Truth compels me to say that appearances were distinctly against that pump—but it worked perfectly!

(7) And now a few words about Lord Rayleigh's results. Before the work upon nitrogen was begun, he had determined the ratio between the densities of hydrogen and oxygen. Three different methods were used for the preparation of oxygen: (*a*) by heating a mixture of potassium and sodium chlorates, (*b*) by heating potassium permanganate, (*c*) by electrolysis. Five weighings of chlorate oxygen yielded figures ranging from 2.6273 to 2.6266 grams; three of permanganate oxygen, figures ranging from 2.6273 to 2.6270; electrolytic oxygen gave the figures 2.6271 and 2.6272. Reduced to standard conditions, these



In the sketch, the iron rod, with its points at C and B, passes through a contracted portion (G) of the upper glass chamber, where a tight joint is made with stout rubber tubing, wired down and covered with a mercury seal. A similar connection is made with the lower chamber at H. The lower portion of each chamber is filled with pure mercury, as is the connecting tube FF. At D is a connection with the Töppler pump; at E the connection with the balloon and the gas reservoir. J is a trap where can be collected any mercury whose surface may have become fouled. K is connected with the adjustable mercury reservoir.

yield as a mean for the weight of a liter of oxygen: 1.42952 grams.

In the case of nitrogen, samples were prepared from air by three different methods: according to the method employed, average weighings of 2.3103, 2.3100 and 2.3102 grams, respectively, were obtained. "Chemical" nitrogen, prepared by five different methods, yielded average weighings of 2.3001, 2.2990, 2.2987, 2.2985, 2.2987 grams, respectively. The mean of the former is 2.3102 grams, of the latter 2.2990 grams—differing therefore by about 1 part in 205. Assuming the density 20 for argon (as compared with nitrogen = 14), this indicates the presence of about 6.91 cc. of the heavier gas in one liter of atmospheric "nitrogen," or of about 8.74 cc. of argon in each liter of air. Later results showed that the percentage by volume is a little greater: 0.937.

To give some idea of the remarkable accuracy of these results when the difficulties surrounding their attainment are taken into account, I would suggest that you be called upon to determine the *exact* percentage content of a solution of common salt by means of a huge pycnometer which weighed, say, 500 grams, yet had a capacity of only 2 cc. Bear in mind that such a determination would involve almost none of the difficulties connected with temperature- and pressure-measurements which are a necessary concomitant of work with gases—and then note, nevertheless, how your courage would ooze away!

(8) The removal of nitrogen from a mixture of that gas with argon, whether by Lord Rayleigh's method or by Ramsay's, was comparatively easy and rapid until the volume had been reduced to but a few per cent. of that at the beginning; then progress became slower and slower. In addition, the likelihood of the glass apparatus giving way, with all that *that* involved, was nerve-racking. Lord Rayleigh's electric arc and Ramsay's furnaces subjected bulbs and tubes to a severe stress. The latter devised an ingenious apparatus by means of which impure argon was drawn from a reservoir, passed over red-hot magnesium, red-hot copper, red-hot copper oxide, caustic potash and phosphoric anhydride, in turn, and then restored to the reservoir—all without coming in contact with anything except these reagents, glass, rubber and mercury! (Rubber connections had to be used where hard-glass tubes were joined to those of soft glass.) No air was allowed to enter the apparatus and no argon to escape, and yet the enclosed gas was kept continuously moving through the system of purifying tubes. This circulating apparatus was often kept going for two days or more on a stretch, while samples drawn off from time to time and weighed, showed that the density of the residual gas was slowly rising—or, if helium was being purified, slowly falling. Sparking-tubes were also constantly brought into use to note the fading of the nitrogen spectrum.

(9) The methods developed for the isolation and purification of argon stood Ramsay in good stead when "cleveite gas" came to be studied. To secure a large volume of argon in pure condition had become merely a question of time: there was plenty in the atmosphere; but from whence was any considerable volume of helium to come? Laboratory technique had to be yet further refined and, at last, when there were separated from argon—*and from each other*—four gases whose volume combined was not as much as 1 part in 500 of argon, it is no wonder that a chorus of praise arose from Ramsay's contemporaries. To use liquid air as a cooling agent was, at that time, not uncommon; to produce liquid *hydrogen* in quantity and to

employ it to render neon non-volatile while the helium with which it was mixed was being completely removed, was certainly something new in laboratory technique. The separation of minute quantities of krypton and xenon from argon was another triumph of patience and manipulative skill.

(10) It is hazardous always to indulge in comparisons. Lord Rayleigh possessed to an extraordinary degree the power of devising simple means to produce desired results. Whether he possessed anything comparable with Ramsay's skill in constructing before the blowpipe, and later, manipulating delicate pieces of glass apparatus, I am in doubt. Both men were doubtless highly ingenious: Lord Rayleigh in avoiding difficulties, Ramsay in overcoming them. Each possessed a charming personality—was blessed with a fund of humor and a delightful courtesy. To offer genuine hospitality to the stranger, to show generous appreciation of his efforts, however modest, seemed to be instinctive with each of them. To have enjoyed a friendship such as they bestowed is, to this writer, a source of pride and will always keep alive towards them a profound sense of gratitude.

BELLADONNA PLASTER.

STANDARDS AND TESTS.

BY FRED B. KILMER AND F. L. HUNT.

There is a long, long trail of history behind such a commonplace thing as a Belladonna Plaster.

Through the maze of legend and written history, we find that the cave man and the nomad had, in some way, gathered a knowledge of the Narcotic Solanums, and applied them for their pain-relieving power.

Hyoscyamus and the Daturas, the famous Mandragora and the Belladonna, have been the pain-relieving Nightshades of widely separated primitive races. The leaves of these plants were applied as poultices, their juice was spread on skins, or made into salves and then spread as a plaster.

Somewhat interesting is the fact that when the Spanish invaded South America, they found the Indians applied a compound of stramonium and pepper as a pain-dispelling poultice or plaster. Here perhaps is the primitive origin of the now popular Belladonna and Capsicum Plaster.

In running through the ages it is of further interest to note that men have, from the beginning, gathered the Narcotic Solanums into a group, owing to their peculiar pain-relieving power, and to them they applied a group name that in widely separate tongues works out into "Nightshade." Further, we find that whatever species of Nightshade may have been peculiar to a country, it was the equivalent of the Narcotic Nightshades of other lands.

Thus, the Datura of India, the Mandragora of Syria, the Hyoscyamus of Egypt, and the Belladonna of Europe, appear confusedly in literature and lore as equivalents in properties and in name. In our own land, the *Solanum nigrum* is quite commonly called Belladonna, and with the Zuni Indians, the *Datura meteloides* is "Indian Belladonna."

In an historical study, a plaster made of any Narcotic Solanum, may be considered as equivalent of a present day Belladonna Plaster.

The use of lead bases for plasters goes back at least fifty centuries. The Diachylon mass, formulated by Menecrates (A.D. 1), is still in use. India-rubber mass plasters are of American origin, beginning about the middle of the 19th century.

The pharmacist is quite apt to look upon the commonplace belladonna plaster as one of the many jokes in medicine. The up-to-date physician looks upon them as harmless, possibly useless.

It seems hardly possible that belladonna plaster could have held its place through the ages if either of these conclusions were correct. It is a notable fact that more belladonna plasters are now being used to relieve the ills of mankind than ever before in the history of the world. Of late years some physicians have discarded belladonna plasters, stating that the local application of belladonna in this form was without action.

Dr. H. C. Wood, the noted therapeutist, stated that "when belladonna is applied to a part it acts locally as a paralysant, overpowering the capillary cells, the sensitive motor nerves, and even muscular and glandular cell action."

According to the late Dr. W. C. Caldwell, "belladonna, when applied to the skin as a plaster, liniment or ointment in large quantity, may be absorbed sufficiently rapid to produce all the symptoms that are developed when taken internally." For the relief of pain, he stated that "its anodyne action is a thousand times stronger when applied at the seat of pain than when taken internally. For the relief of pain the plaster is usually better than the liniment or ointment."

In conditions where there is a peculiar susceptibility to the action of belladonna, the application of a belladonna plaster has been known to be followed by the annoying symptoms of dilation of the pupils of the eye, dryness of the throat, rash, and other manifestations of belladonna action.

Authorities state that plasters made with an india-rubber base have, in common, a mechanical action, protection of the part to which they are applied, limitation of motion in the underlying tissues, and support, and that through this action they produce continuous massage. In addition to the foregoing, with a belladonna plaster we would have the continued action due to the medication (belladonna) contained in the mass, thus producing an anodyne and incidentally an action tending to check secretions.

STANDARDS.

Probably from the fact that it was long held that the leaves of belladonna were more active than the root or other parts of the plant, pharmacopœias and formularies prescribed the use of the extract of the leaves in making belladonna plasters.

The root of belladonna was not recognized officially in England until about 1860, when it was recommended for use in liniments. The United States Pharmacopœia, revision of 1880, prescribed the use of a specially prepared extract of belladonna root for use in a plaster. In 1890 this was changed to the extract of the leaves, the revisers stating that they were influenced to select the leaves from

the fact that "there is a greater uniformity in the quantity of alkaloids present in the extract from the leaves than in the extract from the root."

The British Pharmacopœia has quite uniformly favored a plaster made from extract of the leaves.

Just as accurate uniformity of alkaloidal content can be secured in preparations made from the root as in those made from the leaves.

The proper standard for any drug preparation of this character is the alkaloidal content, irrespective of the part used, or the proportion of extract employed. Thus, the British and the American Pharmacopœias, in prescribing an alkaloidal standard for belladonna might, with propriety, allow the use of an extract from either root or leaf, or even the whole plant.

Well-founded objections exist against the use of the extract of belladonna leaf in a plaster. The extract of the leaf does not give as homogeneous a mass as does the extract of the root, especially when used in a compound containing rubber. The chlorophyl produces an objectionable green color, which stains the cloth upon which the plaster is spread, as well as the face of the cloth covering the plaster, rendering it unsightly.

Through public demand, belladonna plasters made from the extract of the root are now in universal use.

The 1840 edition of the U. S. P. was the first to admit belladonna plaster, the formula being—Resin Plaster, 3 ounces, Extract of Belladonna Leaves, $1^1/_2$ ounces. The extract was obtained by percolating the leaves of belladonna with dilute alcohol. The next two editions retained practically the same formula, but the 1870 edition called for extract of the root. Here the plaster mass contained the extract percolated with pure alcohol, and enough Resin Plaster was added to make the total weight represent the original weight of the belladonna root. In the 1880, or sixth edition, the formula remained unchanged.

In the seventh revision (1890), by calculating the amount of mydriatic alkaloids in the extract used, the plaster should contain 0.3% of alkaloids.

The next edition, the eighth (1900), stated that belladonna plaster should contain not less than 0.38%, nor more than 0.42% mydriatic alkaloids. In this edition, following the directions for the preparation of the plaster with a rubber base, is a method of assay. This is the first time an assay process for belladonna plaster is noted in the Pharmacopœia. The method proposed was one which has been found to be successful.

A slightly lower standard is found in the U. S. P. IX (1910), the requirement being that it should yield not less than 0.35%, nor more than 0.40% belladonna alkaloids. This Pharmacopœia became official September 1st, 1916, and its requirements were legal from that date. The above standard for belladonna plaster, however, was subsequently reduced to 0.25%, as we shall see later.

In 1918, as a result of the scarcity of belladonna, and in order that the depleted stocks of belladonna on hand might be conserved for other medicinal purposes the American Drug Manufacturers' Association requested the Committee on Revision of the United States Pharmacopœia to adopt the standard of 0.25%, not only as a war measure, but because this standard had been shown to be of therapeutic value. In this recommendation the Committee on Revision concurred.

The adoption of this proposed standard was a step toward establishing a

universal standard for belladonna plaster. The standard of 0.25% alkaloids conforms to the 1914, or present, British Pharmacopœial requirement. Previous to this, the 1898 British Pharmacopœial standard of 0.5% alkaloids was found to be too high, because cases of poisoning, characterized by impaired vision (dilation of the pupil) and dryness of the throat, had occurred. As a consequence, the British Pharmaceutical Conference approved reducing the standard to just one-half the former strength, and the 0.25% standard was adopted by the British Pharmacopœia in 1914. This is also the standard of the British Codex, the Cuban Pharmacopœia and the Farmacopeia Latino Americano.

The American Drug Manufacturers' Association also recommended that inasmuch as there was no standard for Belladonna and Capsicum Plaster, it should contain 0.125% alkaloids of belladonna and 5% of powdered capsicum. This is half the alkaloidal strength of the plain belladonna plaster.

We give here a table showing the formulas and standards for belladonna plaster as shown in the pharmacopœias of the world so far as we have been able to obtain them.

BELLADONNA PLASTER.

FORMULAS IN VARIOUS PHARMACOPŒIAS.

Farmacopea Nacional Argentina primera edicion, 1898—No formula.

Pharmacopœa Austriaca editio octava, 1906—No formula.

Pharmacopœa Belgica editio tertia, 1906—No formula.

British Pharmacopœia, 1914—Liquid extract of belladonna root—50 millilitres; Resin plaster—137.50 grammes. Standard, 0.25 per cent. of the alkaloids of belladonna root.

Farmacopea Chilena, 1905—Extracto fluido de belladona—treinta partes 30; Emplasta de pez—setenta partes 70; Elemi—quince partes 15; Aceite de oliva—cinco partes 5; Haganse cilindros.

Pharmacopoea Danica, 1907—No formula.

Pharmacopoea Fennica editio quinta, 1914—No formula.

Pharmacopée Francaise Codex Medicamentarium, 1908, Supplement 1920—Extrait de belladone—vingt-cinq grammes 25; Elemi purifie—vingt-cinq grammes 25; Emplatre diachylon gomme—cinquante grammes 50.

Pharmacopœa Germanica, editio quinta. 1910—No formula.

Pharmacopœa Helvetica editio quarta, 1907—Extractum belladonnæ—10; Elemi—10; Colophonium—20; Emplastrum adhaesivum—60.

Farmacopea oficial Espanola septima edicion, 1915—Extracto de belladona—200; Emplasto de pez de Borgona—750; Aceite de olivas—100.

Pharmacopœa Hungarica editio tertia, 1909—No formula.

Farmacopea ufficiale del Regno d'Italia terza edizione, 1920—No formula.

The Pharmacopœia of Japan, 1906, English translation 1922—No formula.

Farmacopea Latino—Americana, 1920—Extracto liquido de belladona—50.0 cc.; Emplasto de resina—137.5 gr.; Contiene 0.25 por 100; de los alcaloides de la raiz de belladona.

Farmacopea Mexicana, cuarta edicion, 1904—Polvo de hojas de belladona (tamiz num. 5)—20; Alcohol, 90%—10; Amoniaco a 22°—1; Cera amarilla—30; Trementina—25; Colofonia—25.

Farmacopea Nederlandica, editio quarta, 1905, supplement, 1910—No formula.

Pharmacopœa Norvegica, editio quarta, 1913—No formula.

Pharmacopea Romana, editio tertia, 1893—No formula.

Pharmacopœa Svecica, 1908—No formula.

Farmacopea Venezolana, 1910—Extracto de Belladona—25.00; Resina Elemi—25.00; Emplasto de Diagiulon gomad—50.00.

Pharmacopœia of the United States, Ninth Decennial Revision, 1916—Extract of Belladonna Leaves—30 per cent. (rubber mass). Standard not less than 0.25 per cent. nor more than 0.30 per cent. of the alkaloids of Belladonna Leaves.

British Pharmaceutical Codex, 1924—Dry extract of Belladonna Leaves—25 parts; Rubber Adhesive Plaster to 100 parts. Standard 0.25 per cent. of the alkaloids of Belladonna leaves.

The U. S. P., Revision IX, established the standard for belladonna plaster in the following language:

> "An adhesive plaster containing 30 per cent. of extract of belladonna leaves and yielding not less than 0.25 per cent. nor more than 0.30 per cent. of the alkaloids from belladonna leaves."

This statement is somewhat ambiguous. As it reads it assumes that an extract of belladonna leaves will be used of such a strength that 30 per cent. of the extract in the mass will yield a mass containing from 0.25 to 0.30 per cent. alkaloids. If 30 per cent. U. S. P. extract were used it would give a mass containing 0.375 per cent. alkaloids.

This standard allows for no variation in the alkaloidal content of the extract. If 30 per cent. extract of belladonna leaves were incorporated in a plaster mass, it would produce a sticky, unworkable compound.

There is no method known to us by which the alkaloid of belladonna leaves can be distinguished from the alkaloid of the root.

The revisers evidently intended to require that the mass should contain not less than 0.25, nor more than 0.30 per cent. of mydriatic alkaloids.

In the manufacture of belladonna plasters on a large scale, uniformity of alkaloidal content and compliance with the alkaloidal standard, are secured by the following procedure:

Each lot of extract is assayed, and its alkaloidal strength placed upon the label. Different lots of extract, of course, vary in alkaloidal content. A table is constructed showing the amount of extract of a given assay (Col. 1) that should be added to a given weight of plaster mass (Col. 4) in order to produce a finished mass meeting the required alkaloidal strength.

Per cent. alkaloid in extract.	Ratio mass to extract.	Per cent. extract in compound.	Extract used for 200 lb. mass.	Per cent. alkaloid in extract.	Ratio mass to extract.	Per cent. extract in compound.	Extract used for 200 lb. mass.
2.00	7.00	12.50	28.57	2.22	7.88	11.26	25.374
2.01	7.04	12.44	28.409	2.23	7.92	11.21	25.256
2.02	7.08	12.38	28.248	2.24	7.96	11.16	25.128
2.03	7.12	12.32	28.09	2.25	8.00	11.111	25.00
2.04	7.16	12.26	27.93	2.26	8.04	11.06	24.878
2.05	7.20	12.195	27.77	2.27	8.08	11.01	24.756
2.06	7.24	12.14	27.624	2.28	8.12	10.97	24.634
2.07	7.28	12.08	27.47	2.29	8.16	10.92	24.512
2.08	7.32	12.02	27.32	2.30	8.20	10.869	24.39
2.09	7.36	11.96	27.17	2.31	8.24	10.82	24.273
2.10	7.40	11.904	27.03	2.32	8.28	10.78	24.157
2.11	7.44	11.85	26.88	2.33	8.32	10.73	24.041
2.12	7.48	11.79	26.74	2.34	8.36	10.68	23.925
2.13	7.52	11.74	26.59	2.35	8.40	10.638	23.809
2.14	7.56	11.68	26.45	2.36	8.44	10.59	23.700
2.15	7.60	11.627	26.31	2.37	8.48	10.55	23.589
2.16	7.64	11.57	26.176	2.38	8.52	10.50	23.478
2.17	7.68	11.52	26.042	2.39	8.56	10.46	23.367
2.18	7.72	11.47	25.908	2.40	8.60	10.416	23.256
2.19	7.76	11.42	25.774	2.41	8.64	10.37	23.151
2.20	7.80	11.363	25.64	2.42	8.68	10.33	23.045
2.21	7.84	11.31	25.512	2.43	8.72	10.29	22.939

ASSAY PROCESSES.

The simplest test to ascertain the presence of mydriatic alkaloids in a plaster, is to extract the alkaloid and apply a drop of a very weak solution to the eye.

Prescott's "Organic Analysis" and Lyons "Pharmaceutical Assaying" were the standard textbooks on alkaloidal assaying at the time of the sixth and seventh editions of the U. S. P. At that time Mayer's Reagent was used in the valuation of the alkaloid, it having been found by workers that it combined with belladonna alkaloids in nearly definite proportions.

In an excellent article on belladonna plasters, by Seward W. Williams and C. E. Parker, in the PROCEEDINGS OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, 1890, the authors advocated the use of Mayer's Reagent, in preference to the gravimetric method, in titrating the alkaloid, on account of the difficulty in purifying the alkaloids without loss. The various other manipulative details are given quite fully, and three processes are outlined for carrying out the plaster assay. Parts of Williams' method are embodied in the present official assay process.

In a private communication, the late Mr. Williams mentioned that he was using a specially adapted centrifugal machine to break up emulsions, whereby he hoped to perfect a simplified process of assay.

Carl E. Smith, in *The American Journal of Pharmacy*, April, 1898, published a method of assay for belladonna plaster which contained some suggested improvements over the Williams and Parker method.

Bennett F. Davenport, in an article in *Red Cross Notes*, Series II, No. 3, 1898, page 10, entitled "Difficulties in the Assay of Belladonna Plasters," stated that "The most generally approved shakeout methods of assay for alkaloids in belladonna plaster, when made with a rubber mass, have certain practical difficulties inherent in the solvents and precipitants used, which render them very liable to yield erroneous results." To eliminate the persistent emulsions formed when the chloroform-alcohol solution is extracted with weak sulphuric acid, he recommended the evaporation of that solution to remove the alcohol, and then redissolving in chloroform, from which the alkaloids are extracted with weak acid in the usual manner. Davenport was also aware of the fact that heat causes loss of alkaloid.

There are difficulties to be encountered in the assay of belladonna plasters, which an analyst experienced in other types of assay would not suspect. In the assay of a plaster one is dealing with a mixture of india-rubber, resin, waxes, pitch and other ingredients. The first precipitation of the rubber from the chloroformic solution of the mass is apt to occlude some of the alkaloids, hence the advisability of redissolving the precipitated rubber mass in a measured amount of chloroform and reprecipitating with exactly four-fifths of its volume of 95% alcohol.

The large bulk of chloroform-alcohol mixture, containing the alkaloids, is extracted with some difficulty. Hence, the advisability of removing nearly all the alcohol by careful evaporation, and then taking up with a fresh portion of chloroform, from which the alkaloids are extracted with 0.5% sulphuric acid, until a portion, when tested with Mayer's Reagent, no longer gives a test for alkaloids. Should there be any alcohol present, it would tend to have a solvent action on the iodohydrargyrate of the alkaloids, and not give the characteristic precipitate.

The mere extraction with the prescribed amount of chloroform in the final extraction, does not necessarily insure the complete removal of the alkaloids. It is good practice to test the third or fourth portion by the evaporation of 1 cc., dissolving in dilute acid and testing with mercuric potassium iodide.

In some respects the eighth edition of the U. S. P. gives more specific directions than the present volume. As an example, the term "weak sulphuric acid," which is employed, is somewhat vague. The eighth edition stated very definitely that 40 parts of normal sulphuric acid, volumetric solution, were to be mixed with 60 parts of distilled water. Sulphuric acid, 0.5% seems to be the strength to use in making the acid shakeouts. Prior to the issuance of the corrections to the present Pharmacopœia, water was directed to be used in extracting the alkaloids from the chloroform-alcohol mixture after precipitation of the rubber. This resulted in the formation of very obstinate emulsions, and this part of the process had to be abandoned, using instead 0.5% sulphuric acid.

In the evaporation of the final chloroformic solution, prolonged heating on the water-bath is to be guarded against. Too much heat results in the transformation of the alkaloids, thereby producing low results. In the final chloroform evaporation, it is advisable to add two or three 1 cc. portions of chloroform to the brownish residue and carefully evaporate, using a current of air to remove the last traces of chloroform. In this manner, any remaining traces of ammonia are eliminated. The eighth revision of the U. S. P. advocated the use of ten drops of chloroform in dissolving the final residue after adding the 5 cc. of tenth-normal sulphuric acid. This dissolves any extractive matter which may have been carried through, and which would not otherwise so readily yield the alkaloid to the dilute acid. However, the chloroform must be completely evaporated from the acid solution, as it interferes with the indicator in titrating. After the alkaloidal residue is dissolved by the tenth-normal acid, dilute with about 50 cc. of cold distilled water.

Methyl red is by far the best indicator for titrating and it is now employed almost entirely in place of cochineal. Two or three drops of the test solution are sufficient.

Critical points to be observed in the assay are:

a. Precipitation of the rubber from the chloroformic solution with exactly four-fifths its volume of alcohol.

b. Complete extraction of the alkaloids from the precipitated rubber mass, and at every other stage of the assay process.

c. Careful evaporation of the final chloroformic solution, and dispelling all traces of ammonia. Prolonged heating to be avoided, as it produces low results.

d. Complete solution of the alkaloids from the final residue in the tenth-normal sulphuric acid.

Notwithstanding the fact that belladonna plaster is a little troublesome to assay, the deterioration of the alkaloidal strength is very slow. The rubber base is ideal, in that while it permits ready absorption of the medication, it also acts as an excellent preservative for the belladonna alkaloids.

In the abstract of proposed changes in the tenth revision of the U. S. P., Part VII (JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, Novem-

ber, 1924, page 1054), the proposed assay process for Emplastrum Belladonnæ appears as follows, except that we have inserted therein our suggestions in italics:

> Emplastrum Belladonnæ. Assay.—Introduce (*about*) 10 Gm. of Belladonna Plaster (*accurately weighed*) into a 100-cc. flask. (If the plaster is spread on fabric, cut the portion to be assayed into strips, weigh accurately, and introduce it into the flask.) Now add 50 cc. of chloroform, and shake the mixture until the plaster is dissolved. Pour the chloroform solution into a 250-cc. beaker and wash the cloth upon which the plaster was spread with two portions of 25 cc. each of chloroform, adding the washings to the chloroform solutions in the beaker. Then wash this cloth with 80 cc. of alcohol containing 1 cc. of ammonia T. S. and pour the washings into the chloroform solution in the beaker. Stir the mixture gently and allow it to stand until the rubber has separated into a compact mass. Dry cloth upon which the plaster was spread, weigh it and subtract its weight from the original weight of the plaster. Pour the chloroform-alcohol solution into a 250-cc. separator, rinse the beaker and rubber with 10 cc. of alcohol and add the rinsing to the separator. Completely extract the alkaloids from the chloroform-alcohol solution by shaking it out repeatedly with weak (*strike out the word "weak" and insert 0.5 per cent.*) sulphuric acid. Collect the cold (*strike out the word "cold"*) washings in a separator and add ammonia T. S. until the solution is decidedly alkaline to litmus paper, and completely extract the alkaloids by shaking out repeatedly with chloroform. Filter the chloroform solution through a pledget of purified cotton, evaporate it to dryness and dissolve the alkaloids from the residue in exactly 5 cc. of tenth-normal sulphuric acid, and titrate the excess of acid with fiftieth-normal sodium hydroxide, using cochineal (*strike out the word "cochineal" and insert methyl red*) T. S. as indicator. Each cc. of tenth-normal sulphuric acid consumed corresponds to 0.02893 Gm. of the alkaloids from belladonna leaves.

ASSAY OF BELLADONNA PLASTER CONTAINING LEAD OLEATE BASE.

Belladonna plaster made with a lead oleate base is not adapted to the same method of assay as the present U. S. P. plaster. Allen's "Commercial Organic Analysis" gives the following method of assay:

> "Fifteen grams of the plaster are dissolved with gentle heat in a mixture of 35 cc. of chloroform and 5 cc. of glacial acetic acid; 70 cc. of 4% sulphuric acid are added, and the mixture warmed and stirred. It is filtered under pressure and the cake of lead sulphate disintegrated and warmed with a mixture of chloroform 10 cc. and 4% sulphuric acid, 10 cc., and again filtered; the chloroform layer is separated from the mixed filtrates and washed twice with 5 cc. of 4% sulphuric acid. The mixed aqueous portions are then rendered alkaline with ammonia and extracted with chloroform, and again shaken into acid and back into chloroform, proceeding as in the assay of other belladonna preparations."

The acetic acid liberates the fatty acids from the soap and decomposes the lead oleate. The chloroform dissolves the fatty acids thus liberated, as well as the resin. The lead is converted into insoluble lead sulphate and removed, while the alkaloids are extracted in the acid menstruum.

The method given in Allen's Commercial "Organic Analysis" is one published by F. C. J. Bird in the *Analyst*, February, 1899.

In the same year, H. J. Henderson presented a paper before the British Pharmaceutical Conference entitled, "The Assay of Belladonna Plaster, B. P., 1898." The details of this process are as follows:

> "Weigh 5 grams of the plaster and introduce it into a stoppered glass separator with 25 cc. of ether; allow the plaster to disintegrate. When the contents of

the separator present the appearance of an emulsion, add 5 cc. of a mixture of glacial acetic acid and water (3 parts of the former to 2 parts of the latter), shake for thirty seconds, and set aside until the acid liquor has completely separated. Draw off the lower layer into a small beaker, and again agitate the ether solution with 5 cc. of the dilute acetic acid of the B. P., and draw off as before. To the united acid liquors in the beaker, add dilute sulphuric acid in excess, stir well, and allow the sulphate of lead to subside. Filter and wash lead precipitate with distilled water until a drop of the filtrate gives no precipitate with Mayer's Reagent. Concentrate the washings to a small bulk, and add these to the contents of the separator."

The remainder of the process consists in following the usual procedure of making alkaline with ammonia and extracting with chloroform. The chloroform extract is purified by shaking with dilute hydrochloric acid, and then neutralizing this acid solution of the alkaloids with ammonia and extracting with chloroform. The chloroform residue is dried and weighed.

Frank X. Moerk published a method for the assay of the Emplastrum Belladonnae U. S. P., 1890, in *The American Journal of Pharmacy*, March, 1899. In this method sulphuric acid is used to convert the lead oleate into insoluble lead sulphate and also to liberate the fatty acids from the soap, thus eliminating these two ingredients. The author used a few milligrams of stearic acid to overcome the persistent emulsions formed when extracting the alkaline solution with chloroform-ether mixture. He found that the stearic acid did not interfere with the accuracy of the results.

The difference between the assay process for plasters containing lead oleate and soap, and the present official plaster which does not contain these ingredients, is the procedure involved in getting rid of these interfering substances. This was accomplished in the different methods by the use of sulphuric and acetic acids. The present U. S. P. method of assay is designed to eliminate the rubber, so that the belladonna alkaloids may be more readily and completely extracted. Although the final object sought is the same, the methods must of necessity differ according to the interfering substances present. Also the judicious use of the miscible solvents eliminates to a great extent the troublesome emulsions.

CONCLUSION.

The alkaloidal standard for Belladonna Plaster adopted by the United States Pharmacopœia, Revision IX, has proven satisfactory, and is quite in conformity with the leading Pharmacopœias of the world.

The assay process found in Revision IX, U. S. P., with the very slight modifications suggested, will be found to give satisfactory results.

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WHY BOTANY AND PHARMACOGNOSY?

BY WILLIAM J. STONEBACK, PH.G.

Some time ago, while entertaining two brother-pharmacists, one of them asked—"Why lay so much stress on Botany and Pharmacognosy in the colleges of pharmacy? Doctors are not prescribing crude drugs and very few of their preparations. It seems a waste of time to require students to study Botany and

Pharmacognosy." With the foregoing question continually in mind, because matriculants ask it also, the title for this paper was not hard to select.

It seems to me as though the majority of students come to our colleges of pharmacy prejudiced not only against this particular subject, but also against a few others. The root of the trouble seems to have started while the student was under the tutelage of a preceptor who experienced some particular difficulty, either fancied or real, in making the required passing grade. Then again, the student seems satisfied with the Botany taught him in the regular High School course. This fallacy is easily dispelled by the professor or instructor by giving a brief examination of the fundamentals required, on the first or second day of the opening sessions. To the chagrin of the professor he will find that potatoes grow on trees and that the microscope is used to look at and count stars.

Were it possible to receive open-minded students the teaching of the subject would be half accomplished. The student acquires the impression that his teachers are not human beings and gets the idea that some demon is hard at work in strewing his otherwise successful college career with insurmountable barriers. Given then a student who is open to conviction and who is not afraid to exert himself in attaining a broader education, the happy medium is attained. He will find others just as human as himself, who, instead of trying to flunk him at every turn, are always ready to extend the helping hand in making the learning and thorough study of this particular subject and its application so clear that its significance cannot be missed.

The study of Botany in a college of pharmacy during the first year of the course is necessary as a foundation for the successful study and perusal of the advanced subject, Pharmacognosy. During the study of botany the student becomes acquainted with the fundamental considerations and structures involved in plant life, at the same time he learns the correct use of another valuable asset, the compound microscope. Remembering then that the height of the pinnacle is determined by the breadth of the base, pharmacognosy is either offered in the second or third year of the college course. If the foundation or the study of botany has been built upon a solid base, the pinnacle or the study of pharmacognosy will rear itself with incredible speed. On the other hand, if not enough attention has been focused on the study of botany, the study of pharmacognosy is so much more difficult.

Another seeming cause for dissatisfaction is the nomenclature involved, the student being required to learn a vocabulary different from the one learned previously. Recently, much has been said about humanizing the study of these subjects by dispensing with the various descriptive terms which facilitate their study. Instead of simplifying the matter it would become more difficult because of the helpless jargon one would find himself in, when asked to describe or define a certain drug. Instead of using the right term, five to ten simpler words would be used, all erroneous and unsatisfactory. The greatest humanization which possibly can be undertaken is that which binds the student and his professors or instructors so close that each will endeavor to do his share by active coöperation with the other, on the work in hand.

The following are the reasons why botany and pharmacognosy should be studied and how the pharmacist may apply the knowledge acquired:

(1) A broader knowledge of nature will naturally follow, making one realize that plants as well as animals live on this earth.

(2) In some localities the use of crude drugs and spices seems to have dwindled perceptibly because the pharmacist has not taken enough time to prevent their becoming worm- or insect-eaten. The wholesaler and jobber usually supply drugs in first-class condition. The pharmacist, who has had a thorough course in pharmacognosy, at least knows how to keep his crude drugs in a salable condition and does not suffer a falling off in sales or profits.

(3) Many pharmacists are handing over their spice trade to the neighborhood grocer. Recently seven prosecutions took place. In each case Carthamus was sold when Crocus or Spanish Saffron was called for. Happily all concerned were grocers and not pharmacists. The fine in each case was $60.00 plus costs for the first offense and up to $1000, plus costs for the second.

(4) Pharmacists located in foreign-settled communities still have and always will have calls for crude drugs as long as they keep them in a salable condition. Statistics indicate that many thousands of dollars' worth of crude drugs are being imported annually into this country. So why not reap some of the profits that others, probably more enterprising, are reaping?

(5) Physicians often consult the pharmacist about the medicinal value of certain crude drugs. If the pharmacist is not acquainted with the drugs he sells he certainly loses valuable talking points, at the same time leaving an element of doubt in the mind of the physician as to whether that particular pharmacist is qualified to fill his prescriptions. Hence, the pharmacist cannot afford to be ignorant from either a financial or an ethical standpoint.

(6) The U. S. Department of Agriculture is always in need of men qualified to carry on drug inspection work. As a preparation for this work, a number of colleges of pharmacy are offering courses in Advanced Pharmacognosy and Technical Microscopy besides the required courses in Botany and Pharmacognosy.

(7) Positions are available with wholesale drug concerns for men qualified in the proper handling and identification of crude drugs.

In conclusion, the pharmacist who has a working knowledge of Botany and Pharmacognosy is better qualified to uphold the food and drug laws and needs to have no fear of continued prosecution for selling crude drugs and spices which furnish him a valuable source of revenue.

ABSTRACT OF DISCUSSION.

Heber W. Youngken expressed his appreciation of the paper. The author's summary of profit from the subjects had been clearly stated, and he added that the study of Latin and Greek is largely for developing the powers of concentration. In his opinion no subjects are better suited for this development than botany and pharmacognosy—they widen the student's power of observation.

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THE HOSPITAL PHARMACISTS' OPPORTUNITIES TO ADVANCE PHARMACY AND TO AID IN THE ATTAINMENT OF THERAPEUTIC SUCCESS.*

BY HENRY J. GOECKEL.[1]

There are certain kinds of pharmaceutical and of pharmacological investigations which the members of the Hospital Section of the American Pharmaceutical Association are best qualified to undertake. It is the purpose of this paper to bring these to the attention of the members.

It should be the aim of members employed in high grade progressive institutions to check up on the therapeutic efficiency and the comparative value of the various types of pharmaceutical products employed by the hospital staff. What is meant by this can best be illustrated by examples of instances observed by the writer in his past experience.

This work can find its greatest success in those hospitals which conform to the spirit of the standards set by the American College of Surgeons for acceptable institutions. This includes the possession of a broad-minded progressive medical staff, good pharmacy and clinical laboratory facilities and good case records, including intelligible and accurate progress notes on the cases.

On the part of the pharmacists it will require a knowledge of pharmacology and an intelligent and sympathetic understanding of what the physician aims to accomplish by the given therapeutic regimen. It will require making bed-side rounds with the physician in charge of the case at times when the results of the treatment can be evaluated. It will also require careful observation on how the product is employed—sometimes the failure is due to the technic of use and not to the product.

It will require of the pharmaceutical staff proper recording of the lot, quality, etc., of all products used and a system of accurate records of the pharmaceutical methods employed in the preparation of the medicaments.

The correct methods to accomplish this is a problem for this Section to work out. Examples of standardizing activities can be found in those of the medical profession in devising suitable case record forms; in the forms and systems of hospital case records; in those provided for recording the results of laboratory work; and in the system evolved by the Society of American Bacteriologists to standardize procedures so as to make the results of bacteriological investigations of comparative value.

ILLUSTRATIONS.

The following observations will illustrate some of the types of problems.

The first is the open question of the most practical base for ointments; whether it is a petroleum, an oleaginous vegetable or animal product; or a saponaceous or a lanolin type of base. Each one has its advantages and its disadvantages. The tendency in recent years, especially in hospitals, has been to use the petrolatum products for the base. It is the writer's opinion based upon personal observations that certain established brands have not at present the bland

* Section on Practical Pharmacy and Dispensing, A. PH. A., Buffalo meeting, 1924.

[1] Consulting pathologist, Somerset Hospital, Somerville, N. J.

properties by virtue of which they won their reputation. This may be due to a different source of supply, or it may be the result of different methods used in the refining. Here pharmaceutical stability and elegance and the therapeutic efficiency may not coincide.

The writer knows of a case where a physician prescribed a solution of potassium chlorate and hydrochloric acid. Many pharmacists might have accepted the authority of formularies, etc., and prepared a chlorine water as no directions or instructions accompanied the prescription. Knowing the physician to be a gastro-enterologist, an inquiry elicited that he did not even know that two substances could be used to produce a chlorine water. He desired the hydrochloric acid because he was treating a case of achlorhydria and the potassium chlorate was given for its possible gland stimulating effects and to aid in clearing the fetid condition in the patient's mouth. He did not want a chlorine solution. He received what he required.

This is an instance where an established pharmaceutical procedure might have been employed hastily and it would not have answered the therapeutic end desired.

Such a simple product as a zinc oxide ointment may be the cause of a pharmacist losing his reputation for reliability. An instance of this kind occurred where the physician wished the antacid demulcent effects of such a preparation for a person having an eczema. The writer took a resublimed, highly diffused zinc oxide, rubbed it to a perfect cream with a small quantity of oil and then worked in the lard, which the physician designated for the base. Another pharmacist who considered it an unbusiness-like procedure to use a high-priced zinc oxide, when a considerably cheaper commercial article was available, and who did not approve of wasting time in triturating with oil, prepared a nice gritty ointment. The result was that the physician insisted that a serious mistake had been made in the second lot of the ointment. The inflammation, which was decidedly allayed by the applications from the first jar of ointment, was much worse after an application of the second lot.

Here in the first preparation pharmaceutical elegance and technic enhanced the therapeutic efficiency. In the second, false economy and careless technic was the cause for therapeutic failure and actual harm.

As is well known, the success of the Carrel-Dakin solution in the treatment of wounds depends as much upon the technic of administration as upon the preparation itself. The writer knows of a case where the solution was used on a heavily bandaged hand. This was kept saturated with the solution until the hand was so severely burned that the patient could not tolerate it any longer.

Here the preparation was not at fault but, decidedly, the mode of administration.

There is another instance where an elegant looking pharmaceutical product was employed. Nice shining, sharp edged salol tablets were given as an intestinal antiseptic. The interne on the service was rather skeptical of the tablets. He had the feces of the patient sent to the laboratory. As a result of this, the recovered salol tablets were returned to the physician. They were apparently unaffected by their passage through the twenty-odd feet of intestines. Their therapeutic effect was apparently nil.

This, incidentally, indicates that there is still much to learn relative to pharmaceutical technic for conserving the therapeutic properties of the medicament.

More recently a physician prescribed ferrous carbonate in the form of Blaud's pills. Desiring to assure satisfactory results he had the patient secure the pills marketed as a specialty by one of the pharmaceutical manufacturers. It was a beautiful pharmaceutical product. If you had cut one of the pills in half, you could have convinced yourself, if you were a skeptic, that a goodly amount of ferrous carbonate was present. But alas, after having taken seven doses of the pills, the patient had an X-ray picture taken of the enteric region. This showed the shadows of the seven pills, all apparently of the same size and sharpness of outline, showing how far each one had traveled from the stomach on its journey back to the outer world. The nice shiny coating certainly preserved the ferrous carbonate, and also protected the pills against dissolution. The therapeutic effect was again nil. I endeavored to secure a print of this film to present before this Section but it had been mailed to a physician in another city.

Investigations along this line are likely to change the viewpoint of the medical profession, as well as the practice in most hospitals of dispensing pills and tablets for every possible purpose. It may have a tendency to add to the problems of the hospital administrators by increasing the cost of pharmaceutical service. It will contribute to the attainment of greater therapeutic efficiency, thereby helping to reduce the average period of hospitalization per patient, with the resulting sociologic advantages of less chronic invalidism and less pauperization.

There is a preparation which was much in use in the vicinity of New York City in the days when the writer was a pharmacist in one of the teaching hospitals of that city. This was known as the compound white lotion (Lotio Alba Co.) and has gone into the discard not because it is lacking in therapeutic value, but because some pharmacists made a product which was not satisfactory. It was either very gritty and poorly diffused or it was caustic, due to an excess of zinc sulphate in the finished product.

Some members of the medical profession, learning that the burning of the skin was due to an excess of zinc sulphate, attempted to overcome this objection by prescribing suspensions of commercial zinc sulphide. This, however, is a very different substance chemically from the polysulphide in the original preparation. It is probably absolutely inert therapeutically and about as smooth as coarsely powdered pumice stone.

The writer while at the hospital where this was extensively employed in the skin clinic produced a very finely dispersed, almost inpalpable, precipitate of the substance on which its therapeutic value depended. This was accomplished by using carefully selected sulphurated potash which was dissolved in distilled water and then heated on a boiling water-bath. Sublimed sulphur was added until it was saturated with all the sulphur it would take up in a clear solution. It was then strained and, under constant stirring, poured into a filtered solution of the zinc sulphate.

The supernatant liquid of the finished product was later tested for a possible excess of zinc sulphate. This was done by adding a few cubic centimeters of it to a solution of sulphurated potash. If by chance a precipitate was produced,

indicating an excess of the zinc salt, this was all precipitated by the additions of more sulphurated potash solution.

As is usually the case if you furnish your staff with a superior product, there was no comment by the medical staff during the entire two years in which it was prepared in this manner. It was only later, when the writer was obliged to give up the position and his successor made the lotion otherwise, that the difference was noted. The staff then insisted a mistake was being made and that the product was not the regular lotion. The improvement had been accepted without comment but the return to the original product was emphatically objected to.

This illustration shows that the investigator must make his own observations and not rely entirely on the physician's report. The members of the medical profession seldom give credit for improvement in results to the preparation, but they are very prompt in noting the results of a poor product and often blame the product when the fault is in the method of using the product or preparation.

SUMMARY.

1. The hospital pharmacist is probably best qualified to undertake pharmaceutical and pharmacological investigations along the lines suggested.
2. This is work which supplements and extends that of the pharmacological laboratories.
3. It will aid in improving pharmaceutical service.
4. It will make therapeusis as applied to the use of pharmaceutical preparations more successful.
5. It will make pharmaceutical service of more value to the medical profession.
6. It will advance scientific and professional pharmacy.
7. It will win for the pharmacist his rightful place on the professional staff of the hospital.
8. It may ultimately lead to the Hospital Standardization Committee's being just as insistent that the responsible members of the pharmaceutical staff should attend the clinical conference meetings as they now insist upon the responsible members of the pathological laboratory staff being present at these conferences.

ABSTRACT OF DISCUSSION.

J. Leon Lascoff commended the paper. **W. J. Stoneback** referred to a pharmacist of his acquaintance who prepared "White Lotion" according to the method followed by the author of the paper, and established a reputation which served as a valuable advertisement for his pharmacy.

William Gray agreed with Dr. Goeckel in general; however each physician presents a problem. The same methods cannot be employed with all physicians; some will take suggestions kindly, others will resent them; suggestions can be made too frequently and unnecessarily.

THE STATUS OF THE HOSPITAL PHARMACIST.

A REPLY BY C. DYNA.

Mr. Swallow in his article on above subject[1] has put before us again a pretty well worn proposition. Every now and then out of the wilderness comes the cry:

[1] JOUR. A. PH. A., January, 1925, pp. 40–43.

"What shall we do to uphold Pharmacy as a profession?" And the echo answers: "What?"

I have read Mr. Swallow's article with much interest. His query has been my own for more than thirteen years. It can be solved very readily, if we have pharmacists in the service with the stamina of the one I am going to speak about hereafter. I am intimately acquainted with him, so can assure you that what I am going to tell you is absolute truth.

Before starting my little tale, I am going to give you my own opinion on Mr. Swallow's points:

Point 1. Of course, they come from the retail ranks, oftentimes because they are looking for an easy job.

Point 2. As a general thing—No.

Point 3. It is up to the pharmacist himself.

Point 4. Unless cast-iron rules cover pharmacists' salaries there is a good chance for increased remuneration.

Point 5. It is a disgrace, and should be so considered by the public, to have any other than a professional pharmacist in charge of a hospital dispensary anywhere. It also is a dereliction of duty on the part of the several State Boards of Pharmacy to allow such a condition to exist.

Mr. Goeckel proposed an association for Hospital Pharmacists. A good idea! I am a staunch supporter and a firm believer in combinations. United, we can make our demands felt and forge ahead; singly, well, we are where we are to-day—just because. But who is going to take the initiative? Hospital pharmacists are scattered all over the union and are far outnumbered by hospital physicians, dietitians, nurses, etc. It seems to me it would have to be more or less of a correspondence association. At the best, salaries are not such as to leave us much for traveling expenses for attending conventions. However, let some one suggest something.

Then again, I recall that a few years ago our own Association proposed a Section for Hospital Pharmacists. Did anything materialize? If so, it has escaped my notice in the JOURNAL, and I am a fairly consistent devotee of our official publication.

Now for my little tale. Not far from where this is written is a State Hospital caring for about twenty-five hundred inmates. The medical staff consists of a medical superintendent and eight other resident physicians, a resident dentist, and a *Resident Pharmacist.* The latter is an heretic in so far as he long ago cut loose from the old druggist's belief of the divine right of all M.D.'s to be considered as somebody far above the ordinary specimens of the genus homo. He insisted upon meeting them and being approached by them as man to man. Heresy of heresies! He considered himself a professional man as much as they, possessing as much and as thorough information of the branches and sciences pertaining to his profession as they in theirs. He was received with tolerance. "If you can't get rid of a nuisance it must be endured." Fortunately, the superintendent of this particular hospital was a man of brains and broad views. It did not take him long to realize that the Pharmacist was a valuable addition to his staff, and he was so accepted—and this without any additions to the rules and regulations governing State Hospitals. So that now this Pharmacist acknowledges no superior

on the staff and holds himself responsible to no one but the superintendent or the one acting as such in his absence.

I have stated that this Pharmacist was an heretic. He had long since discovered that M.D.'s were really made of the same ordinary clay such as produces lawyers, bricklayers, chauffeurs and druggists, and being good-hearted he was willing to help them overcome this handicap of the divine right, but whereat ordinary humans would admit they did not know this or that and ask another ordinary human for information. This, of course, would not do for the privileged few—information desired must be submitted piecemeal or whispered. It was preposterous to think that an ordinary druggist was able to give them an answer to something they were perplexedly hunting for. Nevertheless, it happened that he could and did, and from then on it was not long before questions pertaining to chemistry, physics or other sciences at all related to Pharmacy were submitted to him, and his word was taken and accepted as final. He also has complete charge of the bacteriological and pathological laboratory, and his report on anything—from a urinalysis or a throat culture to a spinal fluid Wassermann—is rarely challenged. He even was requested by "the powers that be" to furnish a list of questions on medical chemistry for the State Civil Service examinations for medical candidates seeking positions. He complied, and then had to rate the papers. And it nearly broke his heart. If I remember correctly he passed but one or two. But think of it—that the chosen few should ever have had to submit first to read and then answer a set of questions propounded by a druggist, and then that he should stand in judgment over them, too. Unbelievable, almost!

Now, as to the emoluments: The political code of the State decrees that the medical staff in any institution in the state is entitled to maintenance, including housing, laundry, food and fuel. In other words, all you have to spend money for is clothing, incidentals, amusements, etc. A day off every week and a three weeks' vacation during the year. The Pharmacist of whom I am writing enjoys all of these privileges. His salary is the same as that of the resident dentist; in fact, the two share a 4-room suite with private bath, in the Administration Building. Could you wish for anything more?

Friends and fellow Hospital Pharmacists, this is a short history of what one of our members has accomplished. What one has done others can do. Come on! Let us get together—let every one put his shoulder to the wheel and we can make the Hospital Pharmacist a recognized and valuable member of the medical staff of every worth-while hospital in these United States.

In conclusion, I beg of you to believe me when I tell you that everything in this brief sketch presents the facts. Furthermore, I do not for one moment think that this is an exception. In all probability, many of the hundreds of thoroughly trained professional men and women pharmacists, devoted to public service, can duplicate the little story I have attempted to relate. My hope is that the faint-hearted may be encouraged, the unsteady be strengthened in purpose, and, that those with a weak spinal column may develop an additional amount of red bone marrow so that they can at least look a rabbit in the face without flinching.

"A Man is as he Thinks he is!"

THE DEPARTMENT OF THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES

("During the war our attention was directed to the Intelligence Tests that were used in connection with our army. Psychologists believe in the value of the Intelligence Tests, and other educators are willing to admit that there is something in them. The Dean of every college of pharmacy is well aware of the fact that too great a percentage of students who enter pharmacy fail to complete their work successfully. For every student who fails there is considerable waste both for the institution and the student. This waste should be reduced to the minimum by the reduction of the percentage of failing students.

"The following article by Dean Wulling points out a way to this accomplishment, and deserves the thoughtful consideration of our educators."— C. B. JORDAN, *Editor.*)

INTELLIGENCE TESTS IN HIGH SCHOOLS.

BY FREDERICK J. WULLING.

In a previous paper I referred to the experiments with intelligence tests made in the College of Science, Literature and the Arts of the University of Minnesota. Other institutions of higher learning have given these tests some attention and it seems that their value is being established as the superior one among a number of ways of determining students' fitness for scholastic work. If these tests are of value in colleges and universities, they ought to be no less valuable in secondary and grade schools. That at least is the position the Minneapolis high-school authorities are taking who are now entering upon an experiment with the Arts College of the University of Minnesota to develop a system whereby the capacity of pupils for higher scholastic work may be forecast while the pupils are still in high school. Dean J. B. Johnston of the Arts College submitted, at a meeting of high-school principals, a proposal to try out a system of intelligence tests designed to show the mental ability of each high school student and to save much time and tax-payers' money in those cases where students cannot possibly go on successfully with higher work, but where that fact would otherwise be discovered only after much delay and cost in the higher schools. Information resulting from the tests will be given only to the respective pupils and their parents. The custom followed at the University, where results of the ability tests are kept in confidence, will be followed by the high schools.

Most of the colleges of pharmacy derive their students from the high schools and soon all Conference schools will be upon the high-school graduation entrance requirement basis. That will be a collective forward step, but in the light of the experience of colleges that have exacted the high-school graduation requirements for a long time, this step should be quickly followed by one which should be based upon an intelligent and reasonable selection of students. The selection would necessarily have to be based upon a number of things, among them, general fitness, character and mental qualification and potentiality.

In a school of pharmacy with which I am intimately familiar and whose entrance requirements for its minimum course of three years are more than merely high-school graduation and whose student body compares favorably with that of other colleges in the fields of pharmacy, dentistry, arts, engineering, etc., an annual average of between twenty-five to thirty per cent. fails to show or to develop

the capacity to go on with the normal progress of the classes. Some have said the "normal" progress in this college is too rapid, but the fact that from seventy to seventy-five per cent. of the students are able to maintain that rate of progress establishes scholastic and economic justification for it. The twenty-five or thirty per cent. who drop out on account of mental inability to carry on work believed by a competent faculty to be of a fair and necessary standard, would be greatly benefited by any method that would save them the year or more it takes in the ordinary way to find out that they are wrongly placed. The colleges too in which such students matriculate lose time and money, of which there is always a scarcity. Dean Johnston, who for a number of years has been preparing and using intelligence tests, has sent letters to certain parents informing them that their children cannot succeed in the University. In practically every case the parents were grateful for the information and set about to place their sons and daughters in more fitting vocations where they are winning success they could not have attained by continuing at the University. There are many cases of the square pegs in the round holes. The intelligence tests tend toward fitting the square peg into the square hole and the round peg into the round hole. It is somebody's business to aid the young men and women in the selection of the field of work in which they can succeed and be happy. In this connection let me quote Dean Johnston: "If we continue to let young men and women go on to certain disappointment and failure, we shall have a most serious injustice to account for. Also, we shall have a serious waste of tax-payers' money to account for." Pharmacy badly needs a better grade of mental material from which to seek recruits. There are among us too many whom medicine, dentistry, education and other fields requiring respectable training and capacity would not have admitted. The collective standard of a profession is made up by averaging the individual standards of its members. The extreme in the standards of pharmacy are too far apart. Some unsuccessful pharmacists have stated that the calling has a distinct duty to perform to keep out those who are unlikely to become successful. I think they are right. A time may come when it will be thought right and proper to establish committees or bodies who will, according to carefully prepared rules for their guidance, determine who may be admitted to pharmacy. Boards of pharmacy might carry out such a function under proper rules.

THE COMMONWEALTH STUDY OF PHARMACEUTICAL EDUCATION.

BULLETIN NO. 4.

This is the fourth of a series of twelve monthly statements to be issued by the staff conducting this study. These bulletins are issued to acquaint the profession with the progress of the study.

The study of nomenclature divides itself into two distinct branches:

The nomenclature I, to be able to read prescriptions
II, to be able to read the U. S. P. and N. F.

I. THE NOMENCLATURE TO BE ABLE TO READ PRESCRIPTIONS.

A prescription is divided into six parts; namely, the *superscription, inscription, subscription, signa, name and address of the doctor* and *name and address of patient.* Only the first four are considered in the nomenclature study.

The *Superscription* consists of ℞, which is an abbreviation for *Recipe,* the imperative

form of *Recipio*, which means "you take" and is printed on nearly all prescription blanks. It has been ignored in this study except to observe the rules of syntax which it governs.

The *Inscription* contains the names of the ingredients and their quantities. The ingredients are written in the genitive case and the quantities in the accusative case.

The *Subscription* gives the working directions to the pharmacist.

The *Signa* gives the directions for the patient to be written on the label by the pharmacist.

The studies showing the Latin necessary to be able to read a prescription are as follows:

A. Latin used in the *subscription* and *signa* of 10,000 prescriptions.

B. Latin used in designating quantities of ingredients found in same 10,000 prescriptions.

C. Latin used in the titles of ingredients found in 16,000 prescriptions.

D. Rules of syntax involved in the prescription.

A. Ten thousand (10,000) prescriptions collected from ten geographical centers were examined to discover what Latin terms were used. These prescriptions were divided into sets of five hundred (500) each, a *pro-rata* sample from each center, and the partitive sampling method was used on them. That is, as each five hundred were examined, record was kept of the number of new terms appearing per five hundred to discover the point of vanishing terms.

Method.—Each term or word was written off as it actually appeared on the prescription on a small piece of paper and these were tabulated together under the proper heading. While the terms were being tabulated, record was kept of the forms in which they were written on the prescriptions. The variety of incorrect forms used by the Doctors was amazing. The outstanding example was that of the Latin word "*chartula*" which was written 22 ways in 437 times used.

The terms "*ana*," "*quantum sufficit*" and "*ad*" in the inscription were included here.

B. The same 10,000 prescriptions as for study A were examined to discover what terms were used in the quantities following the same method. After studying three thousand (3000) prescriptions, no new terms appeared. Only new forms infrequently appearing were encountered after the third thousand.

Sixteen thousand (16,000) prescriptions which include those used in studies A and B were examined to discover what nomenclature was used. The same method was employed as before. Each ingredient as it actually appeared was written on a small piece of paper and these were tabulated together under the official title. In this way, the frequency of the correct Latin title, English title, and synonym was shown. The abbreviations whether written correctly or incorrectly were combined under one heading of abbreviations.

The type of ingredient report shows the frequency of the number of times the Latin title, English title and synonym occur whether written correctly or incorrectly.

All titles which began with the letter "A" except proprietaries were studied. A title to be in correct Latin should be in the genitive case since the inscription of a prescription is in the genitive case. In some instances the synonym was Latinized and therefore it was recorded in two places, first from the standpoint of showing the Latin, secondly of showing the synonym.

The results of the study on titles beginning with the letter "A" were as follows:

1. Times it appeared in correct Latin 12.5%
2. Times it appeared in incorrect Latin 16.5%
3. Times it appeared in correct English 11.1%
4. Times it appeared in incorrect English 3.1%
5. Times it appeared in correct synonym 11.1%
6. Times it appeared in incorrect synonym 4.8%
7. Times it appeared in abbreviated form 40.9%

Here again, the variation in forms for writing titles is very interesting. The ingredient *Aspirin* or *Acidum Acetylsalicylicum* was written in 129 ways; *Calomel, Hydrargyri Chloridum Mite* in 108 ways, and *Sodium Bromide, Sodii Bromidum* in 104 ways.

D. The first fifty prescriptions were translated into full correct Latin then all the rules of syntax were drawn off. This then was repeated for two more sets of fifty each when it developed nothing new appeared. These rules will be part of the finished report.

II. THE NOMENCLATURE TO BE ABLE TO READ U. S. P. AND N. F.

This study divided itself into two groups, namely: 1. The vocabulary or terms: 2. Rules of syntax.

1. The U. S. P. and N. F. were studied and each word or term was recorded with its particular form. This gives us a frequency of terms used.

2. The U. S. P. and N. F. were studied and each rule of syntax which was involved was listed.

PROCEEDINGS OF THE LOCAL BRANCHES

"All papers presented to the Association and Branches shall become the property of the Association with the understanding that they are not to be published in any other publication prior to their publication in those of the Association, except with the consent of the Council."—Part of Chapter VI, Article VI of the By-Laws.

Article IV of Chapter VII reads: "Each local branch having not less than 50 dues-paid members of the Association, holding not less than six meetings annually with an attendance of not less than 9 members at each meeting, and the proceedings of which shall have been submitted to the JOURNAL for publication, may elect one representative to the House of Delegates."

Reports of the meetings of the Local Branches should be mailed to the Editor on the day following the meeting, if possible. Minutes should be typewritten, with wide spaces between the lines. Care should be taken to give proper names correctly, and manuscript should be signed by the reporter.

BALTIMORE.

The January meeting of the Baltimore Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held at the Hotel Emerson, January 27, 1925, John C. Krantz, Jr., presiding.

Dr. Wyatt W. Randall, Chief of the Bureau of Chemistry in the Maryland State Department of Health and a member of the Faculty of the Johns Hopkins School of Hygiene and Public Health, spoke on the subject the "Inert Gases of the Atmosphere."

Dr. Randall sought to emphasize the value of a study of the mental attitude of the investigator towards the facts already known when his research began, and of the influence exerted by newly-discovered facts upon his progress. As an instance, the classical research of Lord Rayleigh which led, through careful studies of the densities of the lighter gases, to the conviction that atmospheric "nitrogen" was not a single form of matter, was discussed at some length. The isolation of argon and later—through the brilliant work of Ramsay—of helium, neon, krypton and xenon, followed as a logical result. The speaker laid stress, however, upon the amazing ingenuity and resourcefulness which characterized the experimental work of the two men, and endeavored to show that only by the combination of such brilliant qualities of mind with rare technical skill could the work have been brought to a successful end.

The election of officers followed, with the following results:

President, Robert L. Swain, 16 West Saratoga St., Baltimore, Md.

First Vice-President, Charles C. Neal, 307 W. Pratt St., Baltimore, Md.

Secretary-Treasurer, B. Olive Cole, Greene and Lombard Sts., Baltimore, Md.

Committee on Membership, Wilmer H. Schulze, Chairman, L. M. Kantner, Miss Carrie G. Mossop.

Committee on Professional Relations, George P. Hetz, Chairman, James A. Black, L. S. Williams.

Committee on Science and Practice of Pharmacy, J. Fuller Frames, Chairman; John C. Krantz, Jr.; W. F. Reindollar.

Committee on Education and Legislation, E. F. Kelly, Chairman; Samuel Y. Harris; J. Carlton Wolf.

The February meeting of the Branch will be held on the 25th at the Hotel Emerson, and the speaker will be Dr. H. H. Lloyd, Professor of Chemistry, Goucher College, his subject being—"Some Recent Views of Atomic Structure."

B. OLIVE COLE, *Secretary-Treasurer.*

CHICAGO.

The 148th meeting of the Chicago Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION was held Friday, February 6, at the University of Illinois, School of Pharmacy. The general subject of the meeting was "Sponges."

President L. E. Warren called the meeting to order and introduced Dr. C. E. Thoraldsen, Professor of Zoölogy at Northwestern University, who gave a very interesting talk on "The Life History of Sponges." He explained the histological structure of sponges, their habitat, cultivation, and characteristics peculiar to them.

C. N. Shuler, an authority on the commercial history of sponges, was then introduced by the President. He followed the talk of Professor Thoraldsen closely by displaying samples of the many different varieties of sponges obtained from the Mediterranean

Sea, Cuban waters, and other tropical seas. He emphasized the commercial value of the sponge in relation to the drug business and how a very profitable business along this line could be worked up by having a well-organized display and bringing it to the attention of the customers.

A rising vote of thanks was given to the two speakers of the evening for their kindness in addressing the Association on this very interesting subject. L. E. WARREN, *President*,
E. N. GATHERCOAL, *Secretary*.

UNIVERSITY OF NORTH CAROLINA.

The twenty-third meeting of the University of North Carolina Branch of the A. PH. A. was held in Gerrard Hall, Monday evening, February second.

Dr. Paul S. Pittenger, head of the department of pharmacodynamics of the H. K. Mulford Co., delivered an address on "Physiologic Drug Assay Methods," which was illustrated by the demonstration of the application of the assay methods of various drugs on test animals and by charts. The lecture was divided into three parts; first, Dr. Pittenger spoke on the necessity of physiologic standardization by showing the wide variation in the activity of preparations made by the same methods from different crops of drugs; secondly, he gave an account of the accuracy and advisability of the use of the various methods for the standardization of those preparations which could not be assayed by chemical methods. In concluding the address the speaker demonstrated the methods of standardization on test animals. He showed the one-hour frog method for the standardization of digitalis, the gold fish method for digitalis, the cock's comb one, the isolated uterus method for ergot, the standardization of the suprarenal gland by the blood pressure method on a dog, and standardization by determining the M. L. D. on guinea-pigs. Dr. Pittenger brought his own test animals from Philadelphia and was assisted in the demonstration by Mr. Cuique of the Mulford staff.

Dr. Pittenger's lecture was particularly interesting and much enjoyed by an audience of nearly five hundred consisting of the faculty and students of the Science Schools at the University and of many physicians and pharmacists from nearby cities.

The Branch wishes to express its appreciation to Dr. Pittenger and the Mulford Co. for the privilege of hearing such an interesting lecture.

E. V. KYSER, *Secretary*.

HISTORICAL COLLECTIONS AND MUSEUMS.

Ernest Spafford said "the knowledge possessed by a historian is not greater than the sum of his sources. History is constantly being made, and in ages yet to come the happenings of to-day, which now may seem commonplace enough, may be of grave and interesting import. "Although there have been in past ages many who recorded events and left those records for others to find, there are many gaps and spaces which probably will never be adequately filled."

So the AMERICAN PHARMACEUTICAL ASSOCIATION has a duty to pharmacy for which a Headquarters Building is essential, and all divisions of the drug trade should coöperate in this valuable and interesting work. Helen E. Fernald, Chief Docent of the University Museum (Philadelphia), said that "times are changing. The museum is beginning to realize its responsibility toward the public. The public is beginning to realize to what great extent the museum is its own and how it can be made to serve many purposes. The museum is fast becoming a workshop for artists, a laboratory of students in art, history or the classics, and ultimate source and authority for many persons of divers interests. It is destined to be used more and more and in increasingly various ways as time goes on. In fact, there seems to be no limit to its possibilities of service except that imposed by the type of collections themselves or the size and number of the staff."

WISCONSIN HISTORICAL MUSEUM DRUG-STORE EXHIBIT.

The Secretary of the National Association of Museums, who was a recent visitor at Madison, Wis., is among the more recent persons to congratulate Curator Brown of the Wisconsin Historical Museum on the old-time drug store exhibit. He said that this drug exhibit was the best single piece in the entire museum. The material for the exhibit was collected during the past fifteen years through the untiring efforts of Dr. Edward Kremers, director of the course in pharmacy at the University of Wisconsin, and arranged by Curator Brown. Many Wisconsin druggists contributed toward the exhibit and it is now probably the most complete assembly of old-time drugs, preparations and drug-store paraphernalia existing anywhere.

Pharmaceutical Era.

ASSOCIATION BUSINESS

AD INTERIM BUSINESS OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION 1924–1925.

Office of the Secretary, 192 Roseville Ave., Newark, N. J.

MINUTES OF THE MEETING OF THE EXECUTIVE COMMITTEE OF THE COUNCIL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION HELD FRIDAY, FEBRUARY 13, 1925, AT THE HOTEL WASHINGTON, WASHINGTON, D. C.

The meeting of the Executive Committee of the Council of the A. PH. A. was called to order by Chairman Beal at 10:15 A.M., Friday, February 13, 1925.

The following were present: Messrs. J. H. Beal, C. W. Holton, H. V. Arny, C. H. LaWall, S. L. Hilton, H. M. Whelpley, W. B. Day, E. F. Kelly, A. G. DuMez, R. P. Fischelis.

The Secretary read a communication from Chairman Scoville of the Revision Committee on the National Formulary in which he called attention to the fact that the appropriation of $1000 made in the budget for the National Formulary would be sufficient for the work of the Committee but would not be sufficient for publication costs and that if the publication costs were included in this appropriation it would have to be enlarged. It was the sense of the meeting that the appropriation mentioned in the budget was for the National Formulary Committee and not for publication charges and the budget was therefore approved as it stood. Chairman Fischelis of the Publication Committee then read the National Formulary contract as made with the Eschenbach Printing Company and upon motion by Arny, seconded by Whelpley, the contract was approved as read, and the President, Chairman of the Publication Committee, and Secretary were authorized to sign the contract. The motion was carried.

It was moved by LaWall, seconded by Hilton, that the Publication Committee be authorized to arrange for proper insurance of electrotype plates of the National Formulary when they are completed. The motion was carried.

Upon request of the Chairman, Treasurer E. F. Kelly read the report of the Treasurer from January 1st to December 31st, 1924. It was moved by Arny, seconded by LaWall, that the report be approved. The motion was carried. (The report will be published in full in the JOURNAL.)

Chairman Fischelis of the Publication Committee stated that a total of $5000 would cover the probable cost of composition and electrotyping of the National Formulary, and it was moved by Whelpley and seconded by Hilton that $5000 or as much thereof as is required be added to the budget for 1925 to cover the production of the National Formulary during 1925. The motion was carried.

The matter of employing solicitors to collect funds for the Headquarters Building was discussed and as this proposition had already been acted upon by the Council by mail vote, no further action was required, excepting to make proper appropriations to continue the Headquarters' Campaign. It was moved by Holton, seconded by Day, that $5000 be appropriated for expenses of the Headquarters' Campaign committee. The motion was carried.

After an informal discussion of the problem of selecting a full-time Secretary, the Committee adjourned for luncheon at 1:00 P.M.

At 2:15 P.M. the Committee resumed its session, the same members being present, and after further discussion of the problem of securing a full-time Secretary, it was moved by Whelpley, seconded by Arny, that the Secretary of the Council be instructed to call for nominations for a full-time Secretary from the members of the Council, and that a vote be taken on the nominations submitted, not later than April 15. The motion was carried.

The question of the appointment of certain Committees of the Association was then discussed and it was decided that the following Committees shall be appointed by the President of the Association:

Committee on Wm. Procter, Jr., Memorial Fund.
Committee on International Nomenclature.
Committee on Coöperative Publicity.
Committee on Prerequisite Legislation.

Committee on Endowment.

Committee on A. PH. A. Headquarters Building.

Committee on Standards for Drugs and Chemical Products.

It was further agreed that the Delegates to State and National Association Conventions shall be appointed by the President.

It was decided that the Committee on Patents and Trademarks and the Committee on the Status of Pharmacists in the Army and Navy be considered Committees of the House of Delegates and be appointed by the Chairman of the House of Delegates.

It was decided that the Committee on Code of Regulations for the Sale of Poisons shall be considered a Committee of the Section on Education and shall be appointed by the Chairman of that Section.

It was decided that the Commission on Proprietary Medicines shall be considered a Council Committee and shall be appointed by the Chairman of the Council.

It was moved by LaWall, seconded by Arny, that the Secretary of the Association be instructed to substitute the word "Council" wherever the word "Board of Trustees" occurs in the By-Laws of the Council or of the Association. The motion was carried.

Secretary Day announced that he had received a communication from Iowa stating that the dates selected for the Des Moines meeting of the Association conflict with the dates of the State Fair and pointing out that it would be advisable to avoid such a conflict. It was moved by Arny, seconded by Whelpley, that Secretary Day be requested to make definite arrangements regarding date, hotel rates, and other details for the Des Moines meeting, and that he be authorized to make a trip to Des Moines, if necessary, to complete these arrangements. The motion was carried.

It was moved by Whelpley, seconded by Arny, that the Secretary of the AMERICAN PHARMACEUTICAL ASSOCIATION make application for affiliation with the American Association for the Advancement of Science, giving full information regarding the AMERICAN PHARMACEUTICAL ASSOCIATION and transmitting a copy of the last YEAR BOOK and the JOURNAL of the Association, as well as a program of the last annual meeting, with the application. The motion was carried.

Secretary Day made a report of the property of the Association located at the College of Pharmacy, University of Illinois, and also read several communications from the International Pharmaceutical Federation. As neither of these matters required definite action, it was moved by Arny, seconded by Kelly, that the report be received. The motion was carried.

President Holton reporting for the Committee on Property and Funds, stated that the matter of the Treasurer's bond had been investigated, and following a discussion of the subject, it was moved by LaWall, seconded by Hilton, that in view of the fact that the funds of the Association are either in registered securities or mainly deposited subject to withdrawal by check, signed by two officers of the Association, the Executive Committee deems the present bond of $15,000 for the Treasurer to be sufficient. The motion was carried.

President Holton then presented the various recommendations regarding the Centennial fund and the Ebert Prize fund. After some discussion of the subject, it was moved by LaWall, seconded by Whelpley, that a certificate be provided for the recipients of the Ebert Prize in accordance with the proposition made to the Council by Dr. Paul S. Pittenger of Philadelphia; the certificate to be given to all living past recipients of the Ebert prize and that in addition a gold medal be provided to be awarded in the future as the Ebert Prize. The motion was carried.

It was moved by Whelpley, seconded by Day that when the die for the Ebert Prize medal is prepared that Dr. H. V. Arny be permitted to purchase, at cost, a gold impression of the medal for himself, and a silver or bronze impression for his co-worker on the research for which he was awarded the Ebert Prize of 1924. The motion was carried.

It was moved by Arny, seconded by Hilton, that President Holton be appointed a special committee, with such associates as he may select, to arrange for the preparation of a die for the Ebert medal. The motion was carried.

At this point, adjournment was taken until 9 A.M.

Chairman Beal called the Committee to order again at 9:15 P.M.

The following members were present: Messrs. J. H. Beal, H. V. Arny, C. H. LaWall, S. L. Hilton, H. M. Whelpley, W. B. Day, E. F. Kelly, A. G. Dumez, R. P. Fischelis. The first order of business was the report of the Committee on Publication. Chairman Fischelis reported

that the Committee had considered the bids from various printing houses for the 1923 YEAR BOOK and recommended that the contract for this publication be awarded to the Eschenbach Printing Company. It was moved by LaWall, seconded by Arny, that the report be accepted and that the contract for printing the 1923 YEAR BOOK be awarded to the Eschenbach Printing Company. The motion was carried.

The matter of consulting advertisers with reference to a possible change in the size of the JOURNAL was discussed and it was moved by LaWall, seconded by DuMez, that the instructions to the Publication Committee to consult advertisers on this matter be construed to mean that certain individuals be consulted by the Chairman of the Publication Committee and that the consultation be of an informal nature. The motion was carried.

It was moved by Whelpley, seconded by Hilton, that the Publication Committee be instructed to prepare invitations for bids for the distribution of the National Formulary V and that the form of bid be submitted to the Council for approval. The motion was carried.

It was moved by Day, seconded by DuMez, that the Council adopt recommendations to have the name of Dr. Lyman Spalding placed on the roster of the Hall of Fame of New York University. The motion was carried.

Dr. Heber W. Youngken, of Boston, Mass., was nominated to fill the unexpired term of the late Prof. Kraemer on the Committee on Pharmaceutical Research. He was unanimously elected.

The Secretary read the following communication from the Philadelphia Branch of the AMERICAN PHARMACEUTICAL ASSOCIATION:

"Prof. Charles H. LaWall,
636 So. Franklin Square,
Philadelphia, Pa.

Dear Prof. LaWall:

I am transmitting to you a resolution adopted by the Philadelphia Branch of the American Pharmaceutical Association with a request that you bring the resolution to the attention of the council at its next meeting.

'That the Council place American Pharmacy on record in an unhesitating manner regarding the unethical and improper manufacture and sale of alleged medicinal preparations which are in reality an evasion of the 18th Amendment.'

Sincerely yours,

Jos. W. E. Harrisson."

After some discussion it was moved by Arny, seconded by Whelpley, that a special committee of three be appointed to draw up suitable resolutions in connection with the matter presented in the foregoing communication. The motion was carried. Chairman Beal appointed C. H. LaWall, H. V. Arny and E. G. Eberle to act on this Committee.

President Holton submitted the following list of Committees for approval and they were unanimously approved by the Executive Committee:

COMMITTEES.

Committee on Wm. Procter, Jr., Memorial Fund: J. E. Hancock, *Chairman;* A. R. L. Dohme, B. T. Fairchild, C. A. Mayo, E. G. Eberle, J. L. Lengfeld, Henry T. Hopkins, Keyport, N. J., W. B. Day, L. E. Sayre, Parker Cook, J. K. Lilly, H. S. Wellcome, C. G. Merrell, Jose' P. Alacan, J. G. Godding, L. C. Hopp, H. M. Whelpley.

Committee on International Pharmaceutical Nomenclature: A. G. DuMez, Otto Raubenheimer, H. W. Youngken, Arno Viehoever, H. C. Wood.

Committee to Coöperate with Committee from A. C. P. F. and N. A. B. P. on Prerequisite Legislation: R. A. Lyman, E. F. Kelly, C. B. Jordan.

Committee on Endowment Fund: H. M. Whelpley, J. H. Beal, C. O. Bigelow, G. J. Godding.

Committee on A. Ph. A. Headquarters Building: J. H. Beal, J. G. Godding, L. A. Seltzer, E. L. Newcomb, C. H. LaWall, H. S. Noel, W. B. Day, W. H. Zeigler, J. L. Lengfeld E. F. Kelly, J. G. Beard, S. L. Hilton, F. H. Freericks, Jeannot Hostmann.

Committee on Standards of Drugs and Chemical Products: B. L. Murray, Elmer E. Wyckoff, J. A. Koch, L. D. Havenhill, E. L. Newcomb, Hugo Schaefer, Eustace H. Gane, W. A. Puckner, John G. Roberts, Otto Raubenheimer, Geo. D. Rosengarten, O. A. Farwell.

Committee on Coöperative Publicity: R. P.

Fischelis, H. V. Arny, E. L. Newcomb, W. H. Cousins, Ambrose Hunsberger.

COMMITTEES ON MEMBERSHIP.

Boards of Pharmacy.—*Chairman*, H. Lionel Meredith, Hagerstown, Md.; H. C. Christensen, Chicago, Ill.; E. Berger, Tampa, Fla.

Food and Drug Chemists.—*Chairman*, H. C. Fuller, Washington, D. C.; L. E. Sayre, Lawrence, Kans.; W. W. Stockberger, Washington, D. C.; C. O. Ewing, Boston, Mass.; Joseph L. Mayer, New York, N. Y.

Wholesale Druggists and Manufacturers.—*Chairman*, A. R. L. Dohme, Baltimore, Md.; Chas. J. Lynn, Indianapolis, Ind.; W. T. Hover, Denver, Colo.; H. K. Mulford, Philadelphia, Pa.; Ralph R. Patch, Stoneham, Mass.; C. P. Van Schaack, Chicago, Ill.

Faculties in Pharmacy Schools.—*Chairman*, A. H. Clark, Chicago, Ill.; Chas. H. LaWall, Philadelphia, Pa.; Hugo H. Schaefer, New York, N. Y.; E. Spease, Cleveland, Ohio; C. W. Johnson, Seattle, Wash.

GENERAL MEMBERSHIP COMMITTEE.—*Chairman*, William B. Day, 701 So. Wood St., Chicago, Ill.

DISTRICT NO. 1.—*Chairman*, John G. Godding, 278 Dartmouth Street, Boston, Mass. *Including* Maine, New Hampshire, Vermont, Massachusetts, Connecticut, Rhode Island.

Connecticut.—*Chairman*, Curtis P. Gladding, Hartford; Levi Wilcox, Waterbury. **Maine.**—*Chairman*, M. L. Porter, Danforth; Alfred P. Cook, Portland; Geo. O. Tuttle, Portland; Chas. H. Howard, South Paris. **New Hampshire.**—*Chairman*, William D. Grace, Portsmouth; George H. Knowlton, Manchester. **Vermont.**—*Chairman*, Urban S. Livingston, Newport; Wellcome B. Eastman, St. Johnsbury; E. G. McClallen, Rutland. **Massachusetts.**—*Chairman*, Theodore J. Bradley, Boston; Irving P. Gammon, Brookline; Florin J. Amrhein, Brookline; Carlton B. Wheeler, Hudson; Charles F. Nixon, Leominster. **Rhode Island.**—*Chairman*, Herbert Haynes, Providence; E. P. Anthony, Providence.

DISTRICT NO. 2.—*Chairman*, Jeannot Hostmann, 115 W. 68th St., New York, N. Y. *Including* New York, Pennsylvania, New Jersey, Delaware, Maryland, Virginia, West Virginia, District of Columbia.

New Jersey.—*Chairman*, Edward A. Wickham, Newark, N. J.; Henry Jorden, Bridgeton; Edgar R. Sparks, Burlington; Harry W. Crooks, Newark; Fred M. Geimer, Maplewood. **Virginia.**—*Chairman*, A. L. I. Winne, Richmond; W. F. Rudd, Richmond; Maude Lambert, Roanoke; T. F. Knock, Petersburg; Samuel Weinstein, Richmond. **West Virginia.**—*Chairman*, Alfred Walker Sutton; G. O. Young, Buckhannon. **New York.**—*Chairman*, J. Leon Lascoff, New York; L. Berger, New York; Edward S. Dawson, Jr., Syracuse, George C. Diekman, New York; Jacob Diner, New York; Otto Raubenheimer, Brooklyn; Henry B. Smith, Brooklyn. **Maryland.**—*Chairman*, C. L. Meyer, Baltimore; James A. Black, Baltimore; R. L. Swain, Sykesville; George E. Pearce, Frostburg. **District of Columbia.**—*Chairman*, Louis Flemer, Washington; Redmond A. Mayo, Washington; H. E. Kalusowski, Washington. **Delaware.**—*Chairman*, John O. Bosley, Wilmington; Reuben M. Kaufman, Seaford; Harry E. Culver, Middletown; Herbert K. Watson, Wilmington. **Pennsylvania.**—*Chairman*, P. H. Utech, Meadville; Joseph W. England, Philadelphia; Charles F. Kramer, Harrisburg; Ambrose Hunsberger, Philadelphia; Louis Saalbach, Pittsburgh; L. L. Walton, Williamsport.

DISTRICT NO. 3.—*Chairman*, Edward Spease, 3051 Scarborough St., Cleveland, Ohio. *Including* Ohio, Indiana, Illinois, Kentucky, Michigan, Missouri and Kansas.

Illinois.—*Chairman*, Wm. Gray, Chicago; Mrs. M. H. Zwick, Oak Park; Fred Metzger, Springfield; N. S. Eichenberger, Peoria,; John C. Wheatcroft, Chicago; Byron Armstrong, Jacksonville. **Ohio.**—*Chairman*, Edward Spease, Cleveland; Waldo M. Bowman, Toledo; Lewis C. Hopp, Cleveland; Theo. D. Wetterstroem, Columbus; A. L. Flandermeyer, Cleveland; F. H. Freericks, Cincinnati; M. N. Ford, Columbus; O. U. Cassady, Youngstown; Elizabeth Jenkins, Dayton; Caswell A Mayo, Cincinnati. **Indiana.**—*Chairman*, F. W. Meissner, Jr., La Porte; C. B. Jordan, Lafayette; Emil Reyer, South Bend; W. H. Rudder, Salem; R. L. Green, Notre Dame; Ernst Stahlhuth, Indianapolis. **Kentucky.**—*Chairman*, Addison Dimmitt, Louisville; J. W. Gayle, Frankfort; Edward L. Pieck, Covington. **Michigan.**—*Chairman*, L. A. Seltzer, Detroit; A. A. Wheeler, Detroit; William C. Kirchgessner, Grand Rapids; Harry B. Mason, Detroit, **Missouri.**—*Chairman*, R. A. Doyle, East Prairie; H. M. Whelpley, St. Louis; H. C. Tindall, Excelsior Springs; Wm. Mittelbach, Boonville; Mrs. Minnie M. Whitney, Kansas City; Francis Hemm, St. Louis; Alfred W. Pauley, St. Louis.

Kansas.—*Chairman*, Mathias Noll, Atchison; L. D. Havenhill, Lawrence; J. S. Chism, Wichita; Maxmillian W. Friedenburg, Winfield; David F. Deem, Stark; Oscar Joseph Schmitz, Atchison.

DISTRICT NO. 4.—*Chairman*, W. H. Zeigler, 188 Tradd St., Charleston, S. C. *Including* North Carolina, South Carolina, Tennessee, Georgia, Alabama, Mississippi, Florida, Arkansas, Louisiana, Oklahoma, Texas, Panama, Cuba, Porto Rico.

Alabama.—*Chairman*, Carl Whorton, Gadsden; W. E. Bingham, Tuscaloosa; Bernard H. Eichold, Mobile; Lawrence C. Lewis, Tuskegee; W. P. Thomason, Guntersville. **Arkansas.**—*Chairman*, Frank Schachleiter, Little Rock; M. A. Eisele, Hot Springs; Maynard H. Potter. Piggot; Miss Mary A. Fein, Little Rock. **Cuba.**—*Chairman*, José Guillermo Diaz, Havana; José P. Alacan, Havana; Alirio Diaz Guerra, Brooklyn, N. Y. **Florida.**—*Chairman*, D. W. Ramsaur, Jacksonville; E. Berger, Tampa. **Georgia.**—*Chairman*, Robert H. Land, Jr., Augusta; Sinclair S. Jacobs, Atlanta; R. A. Rowlinski, Savannah; Robert Thomas, Jr., Thomasville; Earl E. Pugh, Waynesboro. **Louisiana**—*Chairman*, Christian Schertz, New Orleans; Fabius C. Godbold, New Orleans; Adam Wirth, Mew Orleans; Martial B. Casteix, New Orleans. **Mississippi.**—*Chairman*, Henry M. Faser, University; Gus C. Kendall, Meridian. **Texas.**—*Chairman*, J. C. Buckner, Galveston; C. A. Duncan, Dallas; Zeb. W. Rike, Farmersville; Miss Columbus A. Shipe, Nacogdoches. **Panama.**—*Chairman*, Bolivar Jurado, Panama City; Oswald Chapman, Panama City. **Oklahoma**—*Chairman*, D. B. R. Johnson, Norman; Frank A. Dinkler, Hennessey. **North Carolina.**—*Chairman*, J. G. Beard, Chapel Hill; K. E. Bennett, Bryson City; Charles P. Greyer, Morganton; W. W. Horne, Fayetteville; Edward V. Zoeller, Tarboro. **South Carolina.**—*Chairman*, Joseph B. Hyde, Charleston; W. H. Zeigler, Charleston; S. C. Hodges, Greenwood; D. T. Riley, Florence. **Tennessee.**—*Chairman*, William R. White, Nashville; E. V. Sheely, Memphis. **Porto Rico.**—*Chairman*, Narcisco Cabell Cabrero, San Sebastian; Miguel A. Veve, Fajardo.

DISTRICT NO. 5.—*Chairman*, E. L. Newcomb, University of Minnesota, Minneapolis, Minn. *Including* Montana, Wisconsin, Iowa, Nebraska, Minnesota, North Dakota, and South Dakota.

Iowa.—*Chairman*, Al. Falkenhainer, Algona; G. Scherling, Sioux City; Elbert O. Kagy, Des Moines; John M. Lindly, Winfield; Wilber J. Teeters, Iowa City; Geo. Judisch, Ames; Geo. A. Kiedaisch, Keokuk. **Minnesota.**—*Chairman*, G. Bachman, Minneapolis; William A. Abbett, Duluth; Wm. A. Frost, St. Paul; Chas. H. Huhn, Minneapolis; Robert L. Morland, Worthington; J. H. Beise, Fergus Falls; John Nelson, Lake Park; C. M. Judd, Rochester; R. J. Messing, St. Paul. **Nebraska.**—*Chairman*, R. A. Lyman, Lincoln; Henry R. Gering, Omaha; H. C. Newton, Omaha; D. J. Fink Holdredge; Niels Mikkelsen, Kenesaw. **North Dakota.**—*Chairman*, W. P. Porterfield, Fargo; Wm. F. Sudro, Fargo; Oscar Hallenberg, Fargo; Henry L. Haussamen, Grafton. **South Dakota.**—*Chairman*, Anton Hogstad, Jr., Brookings; David F. Jones, Watertown; James Arthur Pool, Redfield; Earl R. Serles, Brookings. **Montana.**—*Chairman*, Charles E. F. Mollett, Missoula; J. W. Seiden, Lewistown; W. R. Montgomery, Butte; Emil Starz, Helena; Frank A. Scheuber, Livingston; Alex. F. Peterson, Missoula. **Wisconsin.**—*Chairman*, E. G. Raeuber, Milwaukee; O. J. S. Boberg, Eau Claire; B. J. Kremer, Fond du Lac; Geo. L. Sontag, Neillsville; H. G. Ruenzel, Milwaukee; W. W. Albers, Wausau; Otto E. Rydell, Superior.

DISTRICT NO. 6.—*Chairman*, Joseph L. Lengfeld, 1505 Gough Street, San Francisco, California. *Including* California, Nevada, Utah, Colorado, New Mexico, Philippine Islands.

California.—*Chairman*, Joseph L. Lengfeld, San Francisco; Franklin T. Green, San Francisco; W. Bruce Philip, Oakland; George H. P. Lichthardt, Sacramento; A. R. Maas, Los Angeles. **Colorado.**—*Chairman*, Charles J. Clayton, Denver; W. T. Hover, Denver; E. G. Fine, Boulder. **Nevada.**—*Chairman*, W. R. Englert, Elko. **New Mexico.**—*Chairman*, Bernard C. Ruppe, Albuquerque; Wayne W. Weitgenant, Raton. **Utah.**—*Chairman*, John Culley, Ogden; W. L. Eddy, Brigham City. **Philippine Islands.**—*Chairman*, Eduardo Castillo, Manila; Juan Rosales Imson, Manila.

DISTRICT NO. 7.—*Chairman*, C. W. Johnson, Coll. of Pharm., Univ. of Wash., Seattle, Washington. *Including* Washington, Oregon, Idaho, Wyoming, Alaska.

Idaho.—*Chairman*, Roy M. Spargur, Twin Falls; Clarence O. Ballou, Boise; John J.

Buehler, Pocatello. **Oregon.**—*Chairman*, Adolph Ziefle, Corvallis; George C. Blakeley, The Dalles. **Alaska.**—*Chairman*, Zachary J. Loussac, Anchorage. **Wyoming.**—*Chairman*, Andrew Edward Roedel, Cheyenne; Charles Tomsik, Sheridan; Ray I. Cook, Casper. **Washington.**—*Chairman*, Charles W. Johnson, Seattle; Geo. H. Guy, Seattle; Cornelius Osseward, Seattle.

DISTRICT NO. 8.—*Chairman*, Charles F. Heebner, Ontario College of Pharmacy, Toronto, Ontario.

Canada.—R. O. Hurst, Toronto; Henry Walters, Ottawa; Alexander Stewart, Guelph.

The matter of life memberships for building fund subscribers who had contributed $1000 or more was discussed. It was moved by Day, seconded by DuMez, that when any $1000 subscriber has paid $200 or more of his subscription he shall be eligible for election to life membership. The motion was carried.

The matter of bringing the YEAR BOOK of the Association up to date was discussed, and Dr. H. V. Arny offered to prepare one YEAR BOOK for the Association as a gift, during the summer of 1926. The offer was thankfully accepted and it now appears that with the 1924 and 1925 YEAR BOOKS both appearing sometime in 1926, that the Association will have caught up on this annual publication.

It was moved by Arny, seconded by DuMez, that a card and circular be enclosed with the next YEAR BOOK when it is mailed to the members; the circular to explain that the recipient of the book is to indicate on the card whether he desires to receive the YEAR BOOK to be issued the following year or not. This motion was carried.

Several of the members referred to the serious illness of former President L. C. Hopp, and the Executive Committee sent a telegram of sympathy to him.

It was moved by Arny, seconded by LaWall, that the Chairman of the Council appoint a Committee of three to consult with the Board of Trustees of the U. S. P. Convention regarding cooperation in the preparation of a Digest of Comments on the Pharmacopœia to be issued in connection with the YEAR BOOK of the AMERICAN PHARMACEUTICAL ASSOCIATION. The motion was carried.

Dr. Beal appointed the following Committee: A. G. DuMez, H. V. Arny, C. H. LaWall.

It was moved by Arny, seconded by LaWall, that the Chairman of the Publication Committee be requested to submit a bill for expenses incurred in connection with the activities of the Committee in securing bids on the National Formulary, YEAR BOOK, etc. The motion was carried.

It was moved by Fischelis, seconded by Whelpley, that the expenses of Editor Eberle in connection with the meeting of the Executive Committee be paid by the Association as the Committee had requested the Editor's presence at the meeting. The motion was carried.

The meeting adjourned at 11:15 P.M.

ROBERT P. FISCHELIS, *Secretary of the Council.*

EARLY PHARMACEUTICAL PUBLICATIONS.

A recent issue of the *Chemist and Druggist* states that M. Eugene Guitard, in his "Two Centuries of the Press in the Service of Pharmacy" gives some details on early scientific and professional journals. The *Journal des Scavans*, which appeared in Paris in 1665, was, says Voltaire, "the father of all the works of this kind with which Europe is now filled." The monthly *Memoire concernant les Arts et Sciences* followed in 1672, but appeared for only two years. In 1754 came the *Recueil periodique des Observations de Medecine, Chirurgie et Pharmacie* (interesting as the first journal specifying the name of this last-named profession), which still existed on the eve of the Revolution. The *Journal de la Societe des Pharmaciens de Paris* (1797) was the first French journal exclusively devoted to pharmacy and chemistry. It ceased to appear in 1799. The oldest existing pharmaceutical periodical in France is the *Journal de Pharmacie et de Chimie.* Its present title only dates from 1842, for in 1815 it was called *Journal de Pharmacie et des Sciences Accessoires*, and at its foundation (in 1809) the *Bulletin de Pharmacie.*

The *American Journal of Pharmacy* was founded in 1825.

EDITORIAL NOTES

Editor: E. G. EBERLE, Bourse Building, Philadelphia, Pa.

Members of the Council, A. PH. A.: JAMES H. BEAL, *Chairman;* S. L. HILTON, *Vice-Chairman;* ROBERT P. FISCHELIS, *Secretary;* CHARLES H. LAWALL, HENRY M. WHELPLEY, H. V. ARNY, A. G. DUMEZ, CHARLES E. CASPARI, W. L. SCOVILLE. *Ex-Officio:* CHARLES W. HOLTON, President; Vice-Presidents, PAUL S. PITTENGER and WILLIAM MANSFIELD; WILLIAM B. DAY, Secretary; E. F. KELLY, Treasurer; W. BRUCE PHILIP, Chairman of the House of Delegates; Editors of the JOURNAL and YEAR BOOK: E. G. EBERLE AND A. G. DUMEZ. Committee on Publications: R. P. FISCHELIS, *Chairman;* H. V. ARNY, PAUL S. PITTENGER, E. F. KELLY, WM. B. DAY, A. G. DUMEZ, E. G. EBERLE.

Collaborators: The members of the Council; the Editor of the YEAR BOOK, A. G. DUMEZ; E. FULLERTON COOK, Chairman, U. S. P. Revision Committee; W. L. SCOVILLE, Chairman, N. F. Revision Committee; the Chairmen of the Sections, A. Ph. A.: PAUL S. PITTENGER, WILLIAM MANSFIELD, JOHN C. KRANTZ, JR., R. S. LEHMAN; W. BRUCE PHILIP, Chairman of the House of Delegates, A. Ph. A.; W. H. ZEIGLER, President A. C. P. F.; CHARLES B. JORDAN, Chairman Executive Committee, A. C. P. F.; H. LIONEL MEREDITH, President, N. A. B. P.; HENRY C. CHRISTENSEN, Secretary, N. A. B. P.

A CORRECTION.

The "Remarks" on page 9 of the January number should have been headed "Remarks on Silver Ion Concentration Studies of Colloidal Silver Germicides" and placed at end of page 18, and the "Abstract of Discussion" on p. 17, should have been given the title of "Abstract of Discussion of Organic Protein and Colloidal Silver Compounds." The two papers were read and discussed at the same session of the Scientific Section.

FIRST AID WEEK.

The week of March 16 is "First Aid Week," which had its inception four years ago. Aside from serving the public, there are opportunities for impressing it with the service of pharmacy.

William Feather, "Business Philosophy" in *Philadelphia Public Ledger*, says that "too many of us get the idea we know all we need to know. This is a mistake. No man knows so much that he cannot learn more. No man is earning so much that he cannot earn more if he knows more."

"The man who thinks he knows all there is to know about his job is already in his coffin.

"The man who opens his mind to knowledge is on his way to a better job and to a keener enjoyment of life. If you keep your mind open it will keep you young, and if you keep your mind young your body will keep young. Feed your mind with new ideas."

DIPHTHERIA AT NOME.

At Nome, in Alaska, diphtheria became prevalent. Such antitoxin as was available was old, and even this was quickly used up. Pleas were sent for millions of units of fresh antitoxin. The little village, with some seven hundred white and three hundred Eskimo inhabitants, including two hundred children, was icebound. The antitoxin must perforce be carried to it by dog teams or by aeroplane. Now began one of those dramatic races with death that holds the mind of man spellbound. Day by day the press chronicled the slow movements of the fastest dog teams in Alaska en route to Nome. Day by day the public awaited the message that the siege of the elements had been lifted and that the aeroplanes were on their way and we know that with diphtheria each day, indeed, each hour, of delay may mean the difference between life and death. But bear in mind one fact. In time of stress the world turns to scientific medicine and discards every shred of trifling doubt. The incident at Nome is a catastrophe—but it has served a good purpose in dramatizing for the world the service of medical science. *Jour. A. M. A.*, February 7, 1925.

The incident also has pointed to the importance of coöperation and the service of pharmacy.

PERSONAL AND NEWS ITEMS.

Dr. I. M. Kolthoff, who was elected an honorary member of the American Pharmaceutical Association at the meeting in Buffalo, wishes to be remembered to the members with whom he became acquainted while in this country. He fully appreciates the kindnesses and hospitalities extended to him, and evidently,

from the tone of his letter, it is his intention to again visit in the United States.

Harry S. Noel, whose tour throughout the West and Northwest and to the Pacific Coast last year will be remembered because he was eminently successful in his presentations before the various pharmaceutical bodies. For this year he has invitations to visit in the East and in the Northeast. He left home about the 1st of March, and his visit includes the following stops: Rochester, Syracuse, Albany, New Haven, Boston, Providence, and New York.

Mr. Noel is a former chairman of the Section on Commercial Interests, and on a number of occasions has delivered interesting addresses before that section.

John H. Webster, a former President of the N. A. R. D., was a candidate for Detroit School Inspector at the recent election, the results of which are not known at this writing. Mr. Webster is an active participant in the annual meetings of the American Pharmaceutical Association, and those who know him are confident that he will make a most efficient officer for Detroit, if elected.

Frank Rapecis, for 21 years inspector for the New York State Board of Pharmacy, has resigned this position, and is now engaged in business on his own account. The New York State Board of Pharmacy, at its January meeting, presented Mr. Rapecis with an engrossed set of resolutions testifying to their high regard.

Alphonso Major will celebrate his 77th birthday on the Pacific Coast, where he is spending a few of the closing winter weeks.

Mr. and Mrs. Francis E. Holliday and **Mr. and Mrs. Warren L. Bradt** have remembered their friends with cards mailed from Gibralter.

David F. Jones, of Watertown, S. Dak., has established the D. F. Jones Fellowship, and the recipient is **Prof. Anton Hogstad, Jr.** This scholarship was prompted by the work done on the American Wormseed problem by Prof. Hogstad, and is to encourage the spirit of pharmaceutical research. Mr. Jones desires that Prof. Hogstad continue his studies for the doctorate degree, and this he will do at the Graduate School of the University of Minnesota.

Dr. Wm. M. Jardene, Past-President of Kansas State Agricultural College, is the new Secretary of Agriculture. Those who know him best say that he is by birth, training, and experience, well equipped to discharge the duties of his office.

Sister Mary Paul Johnson, a nurse at Charity Hospital, Cleveland, and a graduate of the School of Pharmacy of Western Reserve University, led the list of successful candidates for registration as pharmacists at the recent meeting of the Ohio State Board of Pharmacy. At the School of Pharmacy she was graduated with highest honors.

By the will of Samuel T. Murdock, of Indianapolis, the International Typographical Union is given a home said to be worth $500,000. It is located on four and a half acres of beautiful grounds. The gift may be a suggestion to others in relation to the A. Ph. A. headquarters.

At the recent meeting of the Iowa State Pharmaceutical Association, State Chairman **E. O. Kagy** reported further donations amounting to about $1,000.00.

The Baltimore Branch, A. Ph. A., has on its stationery the following: "Has the Chairman of the Headquarters' Building Fund received your contribution in support of this important project?" This is at the top of the page, and at the bottom this inquiry—"Have you sent in your pledge for the Headquarters' Building Fund?"

The Professional Insurance Corporation of Des Moines, Iowa—an organization writing liability insurance for physicians, dentists and pharmacists—has endorsed the A. Ph. A. Headquarters' Building Campaign and is sending out appeals to the druggists of that section asking them to subscribe to the fund.

W. D. Clark, of Portsmouth, has been reappointed member of the Virginia Board of Pharmacy for another term of five years.

Joseph Jarvis, formerly of Albany, N. Y., has established a drug store, the first in his town, in the new village of Menands, N. Y. Mr. Jarvis was chief pharmacist mate in the Hospital Corps, U. S. Navy, from 1914 to 1919. He was also Manager and Secretary-Treasurer of a Government-owned pharmacy on the Island of Guam.

Dr. Leo. Hendrik Baekeland, former President of the American Chemical Society, has contributed $10,000 to the endowment fund of the Society. This is responsive to a promise made by him that he would donate at least $1.00 for each subscription to the endowment fund as soon as more than 10,000 members had subscribed. This is not only a fine spirit exhibited by the donor, but also by the many contributors of the 18,000 members of the American Chemical Society. It sets an example for other organizations to follow.

The late **Joseph P. Remington** was sketched in a recent issue of the *Philadelphia Evening Bulletin.*

The second annual class of medical noncommissioned officers of the Army Medical Field Service School at Carlisle Barracks received their diplomas on February 15. Among them were pharmacist mate, first class, Custor Cody Foster, of the U. S. Navy, Quantico, Va.; chief pharmacist mate, Joseph Herbert Spalding, Quantico, Va.; pharmacist mate, John LeRoy Ross, U. S. Navy, Philadelphia.

W. S. Parker, for many years Secretary of the North Dakota Board of Pharmacy—an office which he still holds—attended the Minnesota Pharmaceutical Association, and also the Northwest Drug Show. Mr. and Mrs. Parker drove in their car from Lisbon, N. Dak.

Dean L. E. Sayre has entertained the students and members of the faculty at his home during the winter months. The object of these meetings is the promotion of good spirit and fellowship among the students, and of more closely binding the student body and faculty,

For the promotion of research work in urology and pharmacology, the firm of Hynson, Westcott & Dunning, manufacturing pharmacists of Baltimore, have donated the sum of $20,000 to Johns Hopkins University and Hospital of that city. The gift is the first to the research fund obtained by the university's committee which has pledged itself to raise $10,890,000 for the university and hospital before February 22, 1926, which date marks the fiftieth anniversary of the institution.

The terms of the donation which was made by **H. A. B. Dunning,** a member of the firm and also of the committee, provide that the money be kept intact and the interest used for the research work indicated.

Geo. W. Stansfield, of Topeka, Kas., suffered heavy loss by fire which destroyed his building and stock, representing an estimated loss of $85,000, with insurance of less than half that amount.

L. C. Bird, in an article of the *Virginia Pharmacist,* refers to a paper presented by R. S. Breed and Margaret E. Breed before the Society of American Bacteriologists, December 27, 1923, and published in the *Journal of Bacteriology,* in which the early work of Bartolomes Bizio, a pharmacist, is referred to. The following is quoted: "His (Bizio's), discussion is a most interesting forerunner of the great controversy that was to take place about forty years later between Pasteur and Liebig over the nature of fermentation. Bizio shows himself an apt pupil of the great Spallanzani (Locy, 1910), whose work in combating erroneous ideas in regard to spontaneous generation laid the foundation for Pasteur's work in the same field. Bizio's work is also of great interest because it shows him using methods of cultivating chromogenic bacteria on a solid medium (corn meal mush) that antedate Schroeter's similar work by fifty years."

Pasteur was assistant in Balard's laboratory and he was also assistant professor at the Strasbourg School of Pharmacy. An effort to have Pasteur appointed an examiner in pharmacy failed because he was not a qualified pharmacist. Liebig was an apothecary's apprentice; his "Handbuch der Organischen Chemie" is part of Geiger's "Handbuch der Pharmazie" (1839).

A quarter of a century ago a number of State Pharmacal Companies were established; among these the one in Wisconsin has continued to function successfully. The annual report of the organization showed that the assets of the company are $42,172.43 and there is no outstanding indebtedness.

Calvert Drug Company of Baltimore held its annual banquet on February 5. President R. E. Lee Williamson presided as toast-master.

Texas Drug Company, of Dallas, has contracted for the erection of a new building, and will move from the location occupied for about twenty-five years.

Groover-Stewart Drug Company, of Jacksonville, Fla., is erecting a new building. **D. W. Ramsaur** is President of the Company.

Donald McKesson is Treasurer of the recently reorganized N. Y. O. Co.; he was formerly Secretary of McKesson & Robbins.

ANNUAL MEETING OF AMERICAN DRUGGISTS' FIRE INSURANCE COMPANY.

At the annual meeting of American Druggists' Fire Insurance Company the stockholders reëlected Messrs. Chas. H. Avery, Wm. C. Anderson, J. H. Beal, Samuel C. Davis, Frank H. Freericks, L. G. Heinritz, E. B. Heimstreet, Lewis C. Hopp, M. S. Kahn, John D. Muir, Walter Rothwell, Edw. W. Stucky, E. H. Thiesing, Edw. Voss, Jr., Geo. O. Young. The board of directors in turn reelected the following officers: Chas H. Avery, *President;* L. G. Heinritz, *Vice-President;* Frank H. Freericks, *Secretary* and *General Counsel;* Walter Rothwell, *Treasurer;* W. P. Star-

key, *Assistant Secretary;* John H. Linnemann, assistant treasurer. Messrs. Chas. H. Avery, J. H. Beal, L. G. Heinritz, Lewis C. Hopp, Walter Rothwell, Geo O. Young and Frank H. Freericks were reëlected to constitute the executive committee of the company.

The drug trade of the country now has the distinction of a fire insurance company exclusively devoted to its interest which ranks among the million dollar companies. Including the reserves of the company it had on January 1st, 1925, assets over all other liabilities of $1,397,524.79. Statistical tabulation shows that the company, for every dollar of unearned premium policies in force, has available actual net assets of $7.82, in that respect leading all other fire insurance companies.

The board of directors during its session ordered that final arrangements be made to enter the states of North Carolina and Montana for business, and with those arrangements completed the A. D. F. I. Co., will have become regularly established in 43 states. It was also finally decided that in May of 1926 the company would suitably commemorate its twentieth anniversary.

OBITUARY.

BENJAMIN ELLIOTT PRITCHARD.

Benjamin Elliott Pritchard, 76 years old, who was President of the National Association of Retail Druggists, 1903–4, formerly a druggist in McKeesport, Pa., for 30 years, and Secretary of the Western Pennsylvania Retail Druggists' Association, died Friday, February 13, at his home, in Pittsburgh. He was editor of the *Journal, P. R. D. A.*, and for a number of years was Secretary of the Pittsburgh Branch, A. Ph. A.

Mr. Pritchard was born in Pittsburgh and spent his entire life in the Pittsburgh district. He was secretary of the board of directors of the Pittsburgh College of Pharmacy for the last 20 years, a member of the Chamber of Commerce and of the old Smithfield Methodist Episcopal church, taking an active part in the business interests of that body.

He is survived by his widow, Ida Dorland Pritchard; a daughter, Mrs. Abigail P. Fergent, both of Bellevue, and a stepson, Herbert McBride.

DR. WILLIAM F. HILLEBRAND.

Dr. William F. Hillebrand, for the past seventeen years chief of the chemistry division of the Bureau of Standards, Washington, D. C., died on February 7, aged 71 years. He was recognized as a world authority on inorganic analysis, his work on rock and mineral analysis being the leading text in that field. He was born in Honolulu in 1853, and his boyhood was spent in the Sandwich Islands and in California, with visits to China, Java and India. In the early '70's he studied at Cornell and then continued his studies in Germany, under Bunsen. In 1875, with T. H. Norton, he was the first to prepare metallic cerium, lanthanum, and what was then called "didymium." His determination of the specific heats of these metals showed for the first time they were trivalent, and therefore not members of the calcium family as had been supposed.

DR. JOSEF MOELLER.

Dr. Josef Moeller, the well-known professor emeritus of Pharmacognosy and director of the Pharmacognostical Institute of the University of Vienna, died October 4, 1924 at the age of 77. Dr. Moeller's death marks the passing of the last of the original group of exact pharmacognosists among whom the following may be named: Vogl, Wiesner, F. Th. Hanausek, Hoehnel and Nevinny.

Josef Moeller was born at Pápa in Ungarn, March 21, 1848. After graduating from the Gymnasium he studied medicine at the University of Vienna under Hyrtl, Oppolzer, Skoda and Rokitansky, receiving his doctorate in 1873. His microscopical training he acquired in the laboratories of Brücke and Stricker. Dr. Moeller became assistant to Dr. Vogl in 1874 and in 1877 accepted a professorship in the Vienna Technical High School. In 1886 he became professor at Innsbruck and in 1893 professor at Gras in which capacity he continued until 1908 when he was called to Vienna to fill the vacancy caused by the death of the late Dr. Vogl. He continued in this latter position until 1916 when he was forced to retire through ill health.

Moeller's first work dealt with a study of forest trees of which his "Anatomie der Baumrinden" (Berlin 1882) is a characteristic result. Later, he interested himself in the study of the microscopy of foods and drugs and it is in this field of Pharmacognosy that Moeller's

most noted researches were made. Typical of this period of his life are his über "Amerikanische Drogen," die "Rinde von Rhamnus Purshiana," die "Blätter von Duboisia myoporoides," über "Grindelia robusta," über "Yerba Santa," über "Lignum Tupelo," die "Attichwurzel," über "Ipecacuanha," über "Lignum Aloës und Linaloeholz" and über "Digitalis und Verbascum."

Dr. Moeller was a prodigious worker and writer. Besides many scientific articles he was the author of many books relating to Pharmacognosy. He was one of the first, if not the first, author of an illustrated work treating of the microscopical examination of powdered drugs. This is entitled "Pharmakognostischer Atlas" and was published in 1892 while he was professor at Innsbruck. Among other of the works of Dr. Moeller the following may be mentioned. "Mikroskopie der Nahrungs und Genussmittel" (Berlin 1886), "Rohstoffe des Tischler und Drechslergewerbes (Cassel 1884), "Lehrbuch der Arzneimittellehre (Vienna 1893), "Leitfaden der mikroskopisch-pharmazeutischen Übungen" (Vienna 1901), "Lehrbuch der Pharmakognosie" (Vienna 1906) and the aforementioned "Pharmakognosticher Atlas" and "Anatomie der Baumrinden." The work on the "Microscopy of Vegetable Foods" was published conjointly with Dr. Andrew L. Winton, and has been published in both the English and German languages. In 1886–1891 Moeller published conjointly with Dr. Geissler "die Realenzyklopädie der gesamten Pharmazie" (10 volumes) of which the second edition (14 volumes) was published with Dr. Thoms in 1904–1912.

During his life Dr. Moeller held various responsible governmental positions. He was an honorary member of the Deutscher Pharmazeutischen Gesellschaft, a member of the Östereichischen allegemeinen Apothekervereins of Vienna, corresponding member of the Société de Pharmacie of Paris and a member of the Pharmaceutical Society of Great Britain.

ELMER H. WIRTH.

MARION LEROY BURTON.

Dr. Marion LeRoy Burton, President of the University of Michigan, died a victim of over-work and strain. He made a notable record at Ann Arbor, which was a continuation of the fine work he had done at the University of Minnesota and at Smith College. First and last he was an educator, and he gave his life to the colleges of America.

SIR EDWARD THORPE.

Sir Edward Thorpe, professor emeritus of chemistry in the Imperial College of Science and Technology, died in London, February 23, aged seventy-nine years.

Sir Edward was long one of the leading chemists of England and was the author of several works on chemistry. He was a former President of the Chemical Society, British Association for the Advancement of Science, and former chairman of the chemical section of the British Association.

SOCIETIES AND COLLEGES.

GREAT PHARMACY LIBRARY URGED IN HEADQUARTERS BUILDING.

BY ZADA M. COOPER.*

Of the many good reasons why Pharmacy should have a Headquarters Building not the least is the possibility of a great pharmaceutical library. It is true that America already has some splendid libraries, the Lloyd library at Cincinnati, for instance, and also the libraries in some of the older colleges of the East where they have had years in which to grow, but we need a national one.

It may be visionary to say that our Headquarters Building should have a working library that would be second to none anywhere. Its books should be accessible to any responsible pharmacist, that is to say it should be possible for a pharmacist anywhere to borrow any book for a brief period of time, exceptions being made only in case of very rare books. The library should be in charge of a competent pharmacist who could undertake to search these rarer volumes for information on any specified subject. It should be possible for any research worker or other student of pharmaceutical or allied subjects to have the use directly or indirectly of all the available literature.

The libraries of our colleges are spending considerable sums on building up their collections but no colleges can have everything they would like to have. If it were possible to build up a more extensive collection as an

* University of Iowa.

A. Ph. A. library it would be a wonderful asset to pharmaceutical progress. If then the college libraries might have a card catalogue of the books in this library there would be available at all times information about the literature on any subject. Such a library through a system of cards for bibliographic information like that worked out by Dr. Edward Kremers, of the University of Wisconsin, and now being followed at Iowa and other universities could extend its usefulness incalculably.

TESTIMONIAL DINNER TO PRESIDENT CHARLES W. HOLTON, A. PH. A.

The testimonial dinner tendered to President Charles W. Holton of the American Pharmaceutical Association at the "Down Town Club" of Newark by the New York Branch, A. Ph. A., and the New Jersey and Essex County Pharmaceutical Associations, was a success in every way. The attendance was good, and an excellent menu was enjoyed by those present. Mrs. Holton graced the occasion. President Jeannot Hostmann, of the New York Branch, A. Ph. A., presided as toast-master. Before calling on the speakers of the program he presented President Holton with an ivory gavel—a gift of those who participated in this enjoyable affair. Dr. Robert P. Fischelis was chairman of the Committee on arrangements, and the other members were Hugo H. Schaefer, Robert R. Gerstner and Harry W. Crooks.

The toast-master made the introductory remarks, and then presented Prof. H. V. Arny as representative of the New York College of Pharmacy, who spoke on "Holton and the New York College of Pharmacy." He sketched the life of the President from the time that he entered as student to the present, as an official of the *Alma Mater*.

George M. Beringer, Ex-President of the American Pharmaceutical Association, spoke on "Holton—The Association Worker," and in that connection, of the success of the promotions of the New Jersey Pharmaceutical Association, and also within the American Pharmaceutical Association and the New York Branch, in which the honored guest of the evening had a part.

The preceding speakers were in position to speak of the activities of President Holton through their associations with him, but the presentation of "Charles W. Holton as a Citizen" was most interestingly told by the Rev. Alexander Cairns, pastor of the High Street Presbyterian Church, of which Mr. Holton is a member. Evidently Mr. Holton did not expect his friend to tell of his disinterestedness and his many acts of kindness and charity. Throughout the remarks the training and bringing up of Mr. Holton could be discerned by those who had known his father.

The response of President Holton after the conclusion of the address by the last speaker indicated his filial attachment and love, and how well he observed the wise counsel of his father and mother. He paid them a fine tribute and also his helpmeet. The good deeds and accomplishments of a son are sometimes obscured by those of an honored forebear but the pride of giving full credit and acceptance of the benefits as a precious gift does not detract from the good work and deeds of President Charles W. Holton. It was an evening which Mr. and Mrs. Holton will remember with a great deal of pleasure for many years. Those who were present enjoyed the occasion, the program of which was very successfully carried out. Many congratulatory telegrams, letters and messages were received, among them one from all the living ex-presidents, except Ex-President Lewis C. Hopp, who was prevented by serious illness.

MINNESOTA PHARMACEUTICAL ASSOCIATION.

M. B. Kraemer, reporting the meeting of the Minnesota Pharmaceutical Association for the *Pharmaceutical Era*, states that "a large percentage of pharmacists are scientific and professional despite the present-day trend toward extreme commercialism." "This was shown," she says, "by the large attendance at the recent annual meeting of the Minnesota State Pharmaceutical Association."

The Scientific and Practical Section, which joins in the program with the Northwestern Branch A. Ph. A., at the state meetings, was in charge of Dean Frederick J. Wulling. Many interesting papers were presented and discussed at length.

Professor E. L. Newcomb and others related their experiences in the identification of poisonous plants. An interesting paper was presented by David F. Jones of South Dakota on "Building up Pharmaceutical Business on Scientific Lines Where Competition will Find It Hard to Follow." In this contribution Mr. Jones gave his actual experiences, and in making a survey of the profits of different de-

partments he finds that the largest percentage of profit in his store is derived from the prescription department. His contention is that this department can be developed in a pharmacy according to the needs of the community.

Prof. Chas. H. Rogers pointed out how pharmacists can do considerable research work which will have practical value elsewhere. Prof. Gustav Bachman reported on the pharmaceuticals of the market, and called attention to the variation in the quality of cod liver oil, and said that pharmacists should be careful in selecting a brand which has been tested physiologically.

Secretary Samuel C. Henry, of the N. A. R. D., spoke on national legislation, dwelling particularly on the Cramton bill.

Another speaker was Secretary H. C. Christensen, of the National Association of Boards of Pharmacy, who reported on the work of state boards of pharmacy.

There was considerable discussion anent the liquor problems. Almost a unanimity prevailed in expressing that the practice of dispensing liquor on prescriptions has worked an unnecessary hardship on pharmacists, and has been a constant source of annoyance, if not of embarrassment. The expression was quite general that the United States Government should take over the dispensing of liquors.

The third annual Northwest Drug Show, held in the St. Paul Municipal Auditorium, was a success in every way. There was a constant attendance of visitors during the open hours, and it is estimated that more than 500 druggists, and others interested in pharmacy, gathered at the various meetings and attended the drug show.

IOWA PHARMACEUTICAL ASSOCIATION.

The mid-winter meeting of the Iowa Pharmaceutical Association was held in Des Moines. Among the speakers of the occasion were Governor Hammill, H. S. Hansen, George S. Jay, Al. Falkenhainer, Carl Weeks, J. R. Sutter, and Samuel C. Henry. The latter spoke on legislative subjects, and Governor Hammill congratulated the members on their efforts to build their business and profession into the position that they now hold. He also complimented them by saying that the Association had always turned more money into the State Treasury than had been taken out for defraying the expenses of the Board of Pharmacy.

Jospeh R. Sutter spoke on advertising. The points made in the advertising of the firm of which he is a member were related to service and quality. He considered that it was profitable to tie up the advertising of the store with national advertising—by doing so, information is given where products can be secured that are advertised in periodicals. He concluded by saying that "if you really wish to build up a permanent business, do your own advertising of the store and keep in line with national advertising campaigns."

Dean E. O. Kagy, of the College of Pharmacy of Des Moines University, who is State Chairman of the A. Ph. A. Headquarters Building Campaign, reported that Iowa pharmacists and manufacturers had pledged about $20,000 toward this fund. He explained that the location of the building will be determined by the vote of the membership following the completion of the fund. He considered that Des Moines had an excellent chance for securing the building because of its central location. He also said that a sum representing about $50,000 would be donated in case Des Moines is selected for the headquarters.

The following officers were elected: *President*, Denny Brann, Des Moines; *First Vice-President*, J. J. Gillespie, Des Moines; *Second Vice-President*, P. J. Jepson, Newton; *Third Vice-President*, Gus Reppert, Des Moines; *Treasurer*, J. M. Lindley, Winfield; *Secretary*, J. W. Slocum, Indianola.

STATE PHARMACEUTICAL ASSOCIATIONS.

Hotel Delmonte, where California Pharmaceutical Association will hold its annual session, was damaged by fire. The officers of the Association have, however, been advised that the meeting will be taken care of.

South Dakota Pharmaceutical Association is making arrangements to put the Unit plan into operation.

Texas Pharmaceutical Association will have a Drug Show in Fort Worth during its annual convention.

Utah Pharmaceutical Association will meet in June at Cedar Breaks. It is expected that one of the entertainment features will be side trips to Zion National Park, Bryce Canyon, and other scenic points of interest in Southern Utah.

The Virginia Pharmaceutical Association will hold its convention in Staunton, Va., June 23 to June 25. A cordial invitation has been extended to the association by the Chamber of

Commerce and Kiwanis and Rotary clubs of Staunton. Headquarters for the convention will be located at the Stonewall Jackson hotel.

RHODE ISLAND PHARMACEUTICAL ASSOCIATION.

The fifty-first annual meeting of the Rhode Island Pharmaceutical Association was held at Providence. The following officers were elected for the ensuing year: *President*, Franklin N. Strickland, Providence; *Vice-President*, Herbert Haynes, Providence; *Secretary*, William Shallcross, Providence; *Treasurer*, John J. Pastille, Providence; *Executive Committee*, Arthur W. Boston, Joseph L. McDonald, Charles F. Gilson; *Legislative Committee*, Walter J. Batchelder, John B. McGorty, William A. Fortin, William D. Strachin and Earl H. Mason.

The Secretary's report showed a membership of 385, the largest in the association's history, 74 having been admitted during the past year. Frank A. Jackson, Woonsocket, and Harvey I. Leith, Providence, both charter members of the organization, were present. The annual outing of the association will be held during the summer months.

STATE BOARDS OF PHARMACY.

Attorney Jerome Steiner, of the New York State Board of Pharmacy, holds that the New York Pharmacy Ownership Law is valid. He concludes an articles in *The Messenger*, N. Y. College of Pharmacy, by saying: "Due to this legislation the time will arrive when, with few exceptions, none but pharmacists will be engaged in the operation of pharmacies. It is safe to predict that the place of pharmacy among the professions will attain a station exceeded by none. This beneficent law deserves the vigorous support of all pharmacists."

Rhode Island Board of Pharmacy urges registration of pharmacies as well as pharmacists, contending that thereby it will be possible to stop some of the current practices of using certain drug stores for the illegal sale of liquor and a few others for the dispensing of narcotics contrary to law.

Ohio Board of Pharmacy refuses to renew the license of a violator of the prohibition law.

The Texas Board of Pharmacy is now composed of the following members: E. M. Joseph, of Austin; W. A. Klecka, of Temple; A. H. Seely, of Cleburne; M. E. Dooley, of Wolfe City and Wilford Harrison, of Wichita Falls.

Members of the Utah Board of Pharmacy—John Culley and W. A. Hedquist—addressed the Univeristy of Utah Pharmaceutical Association. The Board members were pleased with the advancement being made by the Pharmacy Department.

ANNUAL BANQUET OF BALTIMORE RETAIL DRUGGISTS' ASSOCIATION.

The annual banquet of the Baltimore Retail Druggists' Association will be held at the Hotel Rennert on March 25. The committee of arrangements includes P. J. Boenning, Charles L. Meyer, William H. Pensel, Samuel Y. Harris and G. P. Hetz, with Melville Strasburger as chairman.

NEW YORK ACADEMY OF PHARMACY.

The New York Academy of Pharmacy accepted applications of sixteen additional charter members, at its recent meeting. The election of officers for the ensuing year resulted as follows: *President*, Jacob Diner; *Vice-President*, Robert S. Lehman; *Second Vice-President*, Henry B. Smith; *Third Vice-President*, Samuel S. Dworkin; *Secretary*, Gustave Horstman; *Treasurer*, Peter Diamond.

NEW YORK PHARMACEUTICAL CONFERENCE ASKS COÖPERATION FOR ITS ACTIVITIES.

Asking the coöperation of all pharmacists and retail druggists in the city in furthering the work of the organization, Dr. Jacob Diner and Nicholas S. Gesoalde, President and Secretary respectively of the New York Pharmaceutical Conference, which embraces 18 organizations, have issued a circular letter to the druggists outlining the present and contemplated activities of the conference.

ALBANY COLLEGE OF PHARMACY.

The Education Committee of the Albany Chamber of Commerce has issued a booklet of a hundred pages in which education in Albany is featured and among these institutions the Albany College of Pharmacy. Dean William Mansfield is chairman of the Committee. The business side of education is emphasized; it is an idea that civic bodies in other cities may advantageously follow.

VIRGINIA SCHOOL OF PHARMACY.

The Pharmacy Department of the Medical College of Virginia aims to enlarge its service for those engaged in pharmacy in Virginia. One feature of the plan is to give information regarding scientific, practical and commercial problems, which includes the every-day drug store questions. Dean Rudd has stated that

the extension of this service has been made possible by the coming into the faculty of Roy Childrey, formerly of the Childrey Drug Store.

THE 104TH ANNIVERSARY OF THE PHILADELPHIA COLLEGE OF PHARMACY AND SCIENCE WAS CELEBRATED FEBRUARY 23.

The 104th anniversary of the Philadelphia College of Pharmacy and Science was observed February 23. President William C. Braisted, Deans Charles H. LaWall and J. W. Sturmer made brief addresses. Prof. E. Fullerton Cook, Robert J. Ruth and members of the student body, made reports of activities under their supervision. A musical program, rendered by students of the College, was followed by a One-Act Play, entitled "The Shades of the Alchemists"—the dramatic satire was written by Dean LaWall and presented by the Bachelor in Science and Post-Graduate students.

THE PHARMACIST AND THE LAW.

Because of an intense desire to carry into effect certain purposes there is sometimes a cynical disregard of the principles of justice and equity with which taxation must be animated if it is to be differentiated from arbitrary expropriation. Thoughtful citizens cannot view this disposition with complacency; if it is encouraged Legislatures will feel free in their quest for revenue and get it where there is least danger to the political lives of the legislators.

20,000 BILLS IN STATE LEGISLATURES.

The *National Industrial Council* estimates that 20,000 new laws have been or will be proposed during legislative sessions. Among the "freak bills" pending in legislatures are the following:

"To make it unlawful for a corporation to make any noise interfering with radio broadcasting from 6 P.M. until midnight; requiring state examination and license of beauty doctors; prohibiting the use of paint-spraying machines, so union painters can use more time and get more pay by hand painting; making it unlawful for any employer or worker to offer or accept employment under an individual contract not to join a labor union; requiring corporation employers to file proof with state banking department of ability to meet payroll; requiring motor vehicles to come to a full stop before entering upon paved state roads; providing semi-monthly pay-day for all labor; limiting freight trains to half a mile in length."

STATE LAWS AFFECTING THE DRUG BUSINESS.

In many states regulation and taxation of tobacco and cigarette sales have been under discussion and in some states the proposed measures have become laws. A number of bills in the California Legislature seek to amend the pharmacy law.—Senate bill No. 80 seeks to create a department of narcotic enforcement; No. 180 provides for the establishment of an institution for treatment of narcotic addicts No. 162 seeks to regulate the hours of work of employees in retail drug stores.

Governor Alvan T. Fuller of Massachusetts has signed the bill to dispense with the annual local votes on the question of liquor licensing in each city and town. The law reads that such votes will not be taken, as provided by other statutes, so long as the sale of liquors is forbidden. Pharmacists of Massachusetts are opposing a measure which seeks to consolidate various examining boards.

A bill to prohibit others than registered pharmacists from owning a drug store was introduced in the Minnesota legislature. A companion bill would forbid the use of the term "drug" or "pharmacy" in connection with a store unless it is equipped to fill prescriptions.

A bill which, it is said, is aimed to curb large cut-rate concerns and booze drug stores, has been introduced in the House and now is pending before the Committee on Public Health and Scientific Institutions of the Missouri Legislature. Edward G. Davidson, an insurance agent of St. Louis, is the author of the measure, which would prohibit anyone from owning a drug store who is not a registered pharmacist, nor would it allow the employment of any but a registered pharmacist as manager of the store.

New Jersey Pharmaceutical Association seeks to amend the State Pharmacy law in order to simplify the penalty clause; another bill provides for the registration of pharmacies and limits the use of the terms "Pharmacy," "Drug Store" and "Apothecary Shop" to places so registered by the Board of Pharmacy.

Under the provisions of a bill introduced in the New York Assembly by Edward J. Donohue, Sec. 234, Public Health Law is amended

by permitting a corporation to conduct pharmacies or drug stores if a licensed pharmacist is employed in each pharmacy or drug store. We are not advised relative to this measure—all bills relating to pharmacy should have the approval of State Associations before support is given thereto.

Senate bill 300 and house bill 728 of Pennsylvania Legislature provide that all manufacturers and handlers of alcoholic liquids be required to obtain permits from a State alcohol permit board, to keep records of transactions and permit inspections of books and premises by the board. This bill has been amended, but is still very far from meeting the approval of the drug trade. The Senate passed the bill by a majority of one vote. As first presented it would have required a State permit for the manufacturer or wholesale distributor of any liquid which contains or develops after manufacture one-half of one per cent. or more of any alcohol. Such a requirement embraces any and all medicinal preparations containing one-half or more than one per cent. of alcohol whether manufactured within the State of Pennsylvania or imported into the State. It would include a large percentage of medicinal preparations, non-proprietary and proprietary (patent) medicines. The alcoholic percentages of some of these are given on the labels, but not on all preparations; all are in original packages, and it would be impossible to determine their actual content of alcohol and keep a record of the quantities of alcohol contained in them unless the packages were broken and their contents analyzed. This would be absolutely impracticable.

Regulation of the manufacture and sale of carbonated beverages and still drinks by registration of manufacturers, and establishing standards for bottling, labeling and advertising carbonated drinks, is provided in a bill introduced in the Pennsylvania Senate. The bill would prohibit the sale of any still drinks kept cool by addition of ice. Enforcement of the act is placed under the Department of Agriculture.

Senate bill 235 of Texas Legislature adds to the existing State prohibition law the following definition of intoxicating liquor:—"All distilled, malt, spirituous, vinous, fermented or alcoholic liquors, and all alcoholic liquids or compounds, such as Jamaica ginger, lyko, force, monticello tonic, or other alcoholic preparations by whatever name called, containing more than 00 per cent. by volume of alcohol, and which are capable of being used for beverage purposes, ..."

House bill 58 of Utah Legislature proposes to amend the liquor law so as to require persons who shall sell any alcoholic extracts, essences, medicines or preparations containing in excess of one-half of 1 per cent. of alcohol by volume, to keep a record of all sales in a book for that purpose, which book shall be signed by purchasers.

Wisconsin pharmacists are seeking to pass a model pharmacy law, incorporating the clause which provides that licensed pharmacists should own all drug stores; amendments to the prohibition enforcement law permitting drug stores to dispense liquor on prescription as well as conduct soda fountains, and eliminating the tax on alcohol purchases; and the erection of a pharmacy building at the University of Wisconsin.

THE CRAMTON BILL FAILED.

The Cramton Bill did not become a law. Strenuous efforts were made during the last sessions of the Congress to pass the measure, advocates yielded many points and at the last asked only that the employees of the department be placed under civil service.

ALCOHOLIC BITTERS BARRED IN WISCONSIN.

Soft drink establishments are not permitted to dispense alcoholic bitters according to a recent ruling by Herman L. Ekern, attorney general of Wisconsin. The sale of bitters containing 18 per cent. alcohol intended for medicine, without a perscription, violates the Severson dry act if the bitters are fit to be used as a beverage, the opinion holds. The opinion was requested by Harold J. Marcoe, district attorney of Lafayette county, who reported that a soft drink parlor in his locality was dispensing bitters by the drink. Another opinion affecting soft drink parlors held that the town board has no power under the statute to revoke a license for the sale of non-intoxicating liquors. Another opinion was that an officer who informs the owner of a certain premises that he has a warrant to search the place and exhibits a folded warrant has sufficiently exhibited the same to make its execution legal.

OKLAHOMA REGULATES SALE OF ALCOHOLIC GINGER PREPARATIONS.

A bill has been passed by the senate of the Oklahoma state legislature regulating the sale of Jamaica ginger and other preparations containing as much as one half of one per cent. of alcohol. The bill reads: Section 1—It shall be unlawful for any person to sell, give away,

barter, or otherwise furnish for beverage purposes, or under any circumstances from which the seller or furnisher might reasonably deduce the intention to use the same for such purpose, any extract, medicine or other preparation containing as much as one-half of one per cent. of alcohol by volume.

Section 2—It shall be unlawful for any person to sell, give away, barter or otherwise furnish Jamaica ginger, in any form, containing in excess of one-half of one per cent. of alcohol for beverage purposes, or for any other purpose; provided, however, any licensed apothecary, druggist or pharmacist who shall have executed a bond to the state of Oklahoma, approved by the governor, in the sum of not less than one thousand dollars, for the purpose of procuring pure grain alcohol for medicinal purposes as provided by law, may procure Jamaica ginger for sale for medicinal purposes only. It shall be unlawful for any such apothecary, druggist or pharmacist to keep in excess of one-half gallon of said Jamaica ginger in any form.

In addition to the penalty for a violation of any provision of this act the bond herein mentioned shall be forfeited to the state, and the governor shall require the attorney general to proceed to collect the amount of such bond, the same to be deposited in the state treasury to the account of the general revenue fund.

Section 3—A violation of any provision of this act shall be punished by not less than $50, nor more than $500 and imprisonment for not less than 30 days, nor more than 6 months.—*Pharmaceutical Era.*

VIRGINIA LAW RELATING TO SALE OF TINCTURE OF GINGER.

Section 63 of the Layman Act (Virginia) reads:

63. Jamaica Ginger.—It shall be unlawful for any one but a licensed pharmacist to sell, dispense or give away to the consumer the extract, essence or tincture of Jamaica Ginger, and such pharmacist only upon the prescription of a regular licensed physician, and then only upon the same conditions as ardent spirits are sold under the provisions of this act.

Nothing in this act shall be construed to prevent the manufacture and transportation for sale outside of the State, of the extract, essence, or tincture of Jamaica ginger, into territory where the same may be legally sold.

BOOK NOTICES AND REVIEWS.

The Chemical Publishing Co., Easton, Pa., publishers of chemical and technical books, submit these 3 texts for review:

Our Farm in Cedar Valley. By Edward Hart. 12 mo. 250 pp. Cloth, $1.50.

The author is Professor of Chemical Engineering in Lafayette College; was formerly Editor of the *Journal of the A. Ch. Soc.* and the *Journal An. and Appl. Chemistry.* It is a book on farming, not agriculture, and in pleasant language, intermingled with stories and anecdotes, describes the author's farm—Cedar Valley. As can be expected from such an authority as Professor Hart, a lot of scientific matter is mixed in whenever occasion permits. We want to call special attention to the chapters on: Soil, Trees and Springs in Cedar Valley, Old Time Farming, Old English Farmers and Some Entirely New Ideas. It is a book worth reading and also well suited to take along on your vacation!

The Story of Sugar. By C. F. Bardorf. 12 mo. 191 pp. Cloth, $1.50.

A highly interesting story! The sugar crystal tells the story of its life—in fact of its two lives, *i. e.*, its first experience as a raw sugar crystal and its re-birth as a white crystal. The author succeeded in presenting the technical processes in a popular and attractive form, intermingled with historical facts. This autobiography of a sugar crystal is well worth reading, quite especially by pharmacists to whom Saccharum Album is a true friend.

The Story of the Oak Tree. By Mrs. Ezra Bowen. 12 mo. 127 pp. Cloth, $1.50.

If you stood alone under an oak on a summer's day, and that tree could talk, it would tell you the story as laid down in this book. From the 14 chapters I want to point out the following: Tree Feelings; The Acorn, the Root and the Seedling Oak; The Stem and the Branches; The Leaf, the Flower; How Nature Created the First Plants; Wonders of Wood; Our Beautiful Forests; The Man with the Microscope.

The author chose the Oak Tree as her subject for a nature study, because its story serves as a complete illustration of that underlying fact of nature, the interdependence of all things—the inseparable linkage of animate and inanimate; of atom, molecule, and substance; of soil and plant; animal and man.

Verlag von Julius Springer, Berlin W. 9, the well-known publisher of numerous pharmaceutical, chemical and medical works, submits the following books for review:

Fachausdrücke der Physikalischen Chemie. Von Dr. med. Bruno Kisch, Prof. Universität Köln. 2 Auflage, 100 pp. 95 cents.

During the rapid growth of the youngest offspring of mother chemistry, namely physical chemistry, a host of technical and scientific terms have come into use, which are frequently puzzling not only to the layman but also to the more trained. In the form of an alphabetically arranged dictionary these technical terms are thoroughly explained, so as to be readily understood. On frequent occasions the etymology of the word is also given, as for instance under Fluorescence derived from Fluor = Fluorspar, a mineral on which this property was discovered. Another decided advantage is contributed by the added biographic datas, for instance: Joule = The unit of electrical energy, named after the English physicist, 1818–1889, or Ohm (German physicist, 1787–1859), the unit of electric resistance. A bibliography of 34 books on physical chemistry concludes the text which we can highly recommend as one of the needs in our age.

Kosmetik. Von Dr. Edmund Saalfeld, Sanitätsrat in Berlin. 6 Auflage mit 20 Abbildungen. 136 pp., 95 cents.

The cosmetic art is primarily of hygienic importance and secondarily of an aesthetic character, namely, as to beautifying certain parts of the body, quite especially the visible portions. The author is an authority on this subject and therefore the book is of importance not only to the physician but also to the pharmacist who wishes to keep abreast with the new methods as set forth in the present, sixth edition.

OTTO RAUBENHEIMER, PH.M.

The "Chemical Age Chemical Dictionary"—Chemical Terms. D. Van Nostrand Company, New York. Price $4.50.

The preface of this book, recently published, states that "the vast output of chemical literature at the present time is presenting almost insuperable difficulites to those who attempt to keep abreast of the rapid advances in chemical science. Not the least of these difficulties is the terminology of the subject, for chemical terms are multiplying at a bewildering rate. Frequently too, when a new word or expression is coined it is followed up with an abbreviation or symbol by which it is expressed. One has, in fact, only to glance through the abstracts of the English and American Chemical Societies to realize the difficulty."

The terms relate to organic, inorganic, physical, analytical, and bio chemistry. The terms defined are those in general use and with these, frequently, a number of closely related terms are given. There is no classification into groups, each term being placed in alphabetical order, and the index thereto is arranged accordingly; only the pages given to a letter are designated.

The cross references to terms include, frequently, those of cognate subjects. For example "Ions"—the term is defined, examples are given, and then reference is made to "Electrolytic Dissociation" and "Electrons." "Rythmic Precipitation" is defined and then reference is made to "Liesegang Rings," etc. The different types of isomerism are classed under "Isomerism." Reactions, laws, etc., are given under the names by which they are known; thus—"Hoesch Reaction" under H, not R; "van't Hoff factor" under V. The lines followed in this Dictionary differ from others, as will be noted by preceding. A second volume will deal with "Organic Substances" and this is to be followed with dictionaries of other chemical subjects. The Dictionary of chemical terms will be found useful not only by the experienced chemists but also by students, and is of value in every pharmacy.

Weltwandering Zweier Deutscher. By Herman Thoms and Luise Thoms. Pp. 306. Price 12 marks. Dresden. Verlag von Theodor Steinkopff. 1924.

Prof. Dr. Thoms is well and favorably known to pharmacists, and part of his journey described in the interesting and illustrated volume, brought him into personal touch with American pharmacists. He is director of the Pharmaceutical Institute of the University of Berlin, author of numerous researches in pharmaceutical chemistry, and editor of the "Handbook of Scientific and Practical Pharmacy" now in course of publication. The tour described is that undertaken by his wife and himself—they traveled from Germany to New York, to San Francisco, thence to Honolulu, Japan, China, the Philippine Islands, Singapore, Java, and back to Germany via India and the Red Sea. Professor Thoms has extended a cordial invitation to the pharmacists who will visit Germany this summer.